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NEUROLOGY AND HUMAN EMOTIONS

CHAIRMAN'S ADDRESS

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In the family of medical specialties, clinical neurology has often been regarded as a sibling whose duty is to play an ancillary role to its nearest kin, psychiatry, internal medicine and neurosurgery. It has been facetiously called a fading spinster living in a back bedroom and walking with a soft and gingerly tread. Compared with the lusty, brilliant and occasionally fustian activities of modern psychiatry, contrasted with the brisk, youthful and productive efficiency of neurosurgery and with the dramatic urgencies of internal medicine, the demeanor of clinical neurology, until in very recent years, has bordered on the lustreless.

This is reflected in the impressions entertained about neurology by the public. To many a man-on-the-street, be he well-informed about medicine or otherwise, the specialty of neurology is not clearly defined or even known to exist as such. Very few neurologists have escaped being confronted by this most disconcerting question, "If you are not a brain surgeon or a psychiatrist, then just exactly what sort of a brain specialist are you?"

This seeming modesty on the part of neurology and its desire to keep out of the glaring limelight, while creditable from the standpoint of ethics, is often not entirely a virtue, for it can be a device for concealing certain shortcomings and a cover for an undesirable timidity, reticence or even inertia.

Perhaps, a good example of the "gingerly tread" of clinical neurology is its attitude toward committing itself in a concerted manner on the anatomy, physiology, and pathology of the emotional nervous system. In this day when people are informed in every popular magazine that the emotional problems of man are productive of more misery than all other human ailments combined, when the chief casualties of modern wars are emotional disturbances, neurology has, with one or two notable exceptions, remained almost in a state of "akinetic mutism" in reference to this particular subject.

This charge, if it be accepted as such, does not imply that neurology should stoop to cheap opportunism and produced a flood of empiricisms about the anatomy and physiology of the emotions. However, it seems that it is the duty of this specialty to organize and correlate its available, authentic data on the emotions and to submit them, however incomplete, to both the practising physician and the educated layman, if for no other reason than to temper rank misconceptions and absurd misapplications. The immense popularization of medical knowledge has made many laymen more intelligent and unhappily, in direct proportion, often more credulous. The conservative contributions of neurology to the story of human emotions should be an antidote to that credulity and, in a measure, should offset the bad influence of misguided theories and practices dealing with emotional disorders. An excellent example of this approach to the organic story of the emotions is the recent publication by Dr. Stanley Cobb [1] of his book entitled "Emotions and Clinical Medicine."

The intelligent layman is here to stay. He is interested in the specific mechanisms of the brain as much as, if not more than, he is in what is, through metonymy, called mind. He is as anxious to know where and how emotions operate as he is to learn how and why hydrochloric acid is produced in the stomach. In spite of the current emphasis on unity of mind and body, he remains aware of his emotions as an experience apart from his intellect and his body functions. He is aware of the potent effect of his emotions on his behavior; he senses them as a distinct and powerful internal process and, in a vague manner, he knows of their impact on his visceral organs.

In all this setting of desire on the part of both physician and layman for knowledge about how man emotes and about what structures in the brain and what physiological devices therein produce emotions, practically every standard text on neurology says nothing. Out of 10 textbooks on basic and clinical neurology, the word "emotion" was found in the index in only two of them, and the references were single ones. In two outstanding texts on neurophysiology, that word was indexed with two references, and both had to do with a brief comment on vascular reflexes and hypothalamic discharge, one of these harking back to Sherrington's work in 1900.

In other words, if one is to be guided by modern texts in neurology and neurophysiology, one is justified in concluding that the emotions have no major representation

Read before the Section on Nervous and Mental Diseases at the One Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

1. Cobb, S.: Emotions and Clinical Medicine, New York, W. W. Norton & Co., Inc., 1950.

in the central nervous system and, what is more puzzling, that organic diseases of the emotions do not exist. This nihilistic notion denying an organic substratum for the emotions is carried over into clinical practice where the very term "emotional disorder" invariably connotes a functional disease. Psychosomatic medicine has done little to change this concept, for it has emphasized that the primary factors are always psychogenic and has conceded a pathology only in the end organs controlled by the autonomic nervous system. The two most popular treatises on psychosomatic medicine offer very little on the integration of emotions in the central nervous system, only one of them stressing the significance of the hypothalamus.

The neurologist's reticence in committing himself about emotional anatomy and physiology could be explained by several factors, most of which are my own speculations and interpretations.

First, the neurologist, no matter how much he may deny it, is inhibited by the old concept that to accept emotions as stemming from a true neural mechanism is a threat to the sanctuary of integrality of mind. The doctrine of mind as an indivisible whole is cherished by all schools of psychology and by many psychiatrists for the simple and very practical reason that their techniques lend themselves only to handling the human mind as a nonfractionated unit. Few neurologists have ventured to defy this creed of integrality of mind. It still takes a special courage bordering on academic recklessness to suggest a purely neural or engram basis for mind and emotion in human subjects, when it is known that such a venture will be assailed by the proponents of "personality as a whole" on the one hand and by ultracautious experimental neurophysiologists on the other.

A second factor in causing neglect of the clinical study of human emotions is inherent in the very nature of emotional behavior, probably the greatest deterrent of all. Self-observation of emotional behavier is useless; an impassioned person is too much "beside himself" to study his emotions, and when reflection and insight are good, there are no passions to study. Since the first reports of Lange, the life of feelings remains an elusive thing to the discriminative elements of mind. Nor are objective emotional reactions in others any more readily recognized. The motor expression of emotions is so spontaneous, so infectious, and so liable to interpretation as a total mass pattern conveying a particular inner feeling, that, intrinsically, the analysis of a particular muscular activity is rarely possible. For one human being to make a cool and detached observation of spontaneous emotional behavior in another requires an unusual temperament and special techniques which are difficult to apply.

A third handicap in the neurological analysis of emotional integration is the wide gap which exists between human and animal brain physiology. Experimental neurophysiology has produced a vast amount of data on the emotional nervous system but has been too cautious about recording it as such. Piecemeal, the experimental results have been presented in the guise of rage reactions, grimaces, akinetic mutism, poverty of animation, absence of generalized movements, lack of defensive movements, postural rigidities, respiratory arrhythmias, and a wide array of autonomic discharges, all of which can be called expression of emotional activity. It can also be said that animal experiments on emotions are too objective, while experiments on humans are too subjective, and the results of the two are almost impossible to synthesize.

Finally, there is a fourth factor which retards more complete knowledge of emotional neurophysiology and pathology. It is the unique anatomical complex which is the nexus of the emotions. This term "nexus," which means a bond or tie between the several members of a group or series, is used advisedly in order to avoid the term "center of the emotions" which is eschewed by all good neurologists. The nearer the experimental neurophysiologist gets to this nexus or even the nearer he gets to something which could be regarded as a center, the more he finds himself dealing with a primordial nervous system that knows no nicely myelinated tracts, no clearly defined nuclear masses, but, instead, a veritable bramble bush of reticular and nonmyelinated maze. Here he also finds cortical, subcortical and bulbar pathways of meagre structure involved in elaborate circuits which seem to know no end. The matrix of reticular and tiny nuclear tissues has been successfully penetrated only by the stereotaxic apparatus first devised by Horsely and Clarke, only few modifications of which have so far been applied to humans, namely, in the study of the thalamus by Spiegel [2] and his associates. In animals, the experimental results in terms of emotional physiology are merely tidbits of information which can be assembled only with painful care and with all the misgivings of academic doubt and experimental groping.

These constitute the main handicaps which furnish the neurologist an apologia for failing to bring forth a clear understanding of the organic basis of the emotions.

The reflections recorded here are not a scholarly ensemble or the results of highly organized experimental work, but are rather the homely observations of everyday practice in clinical neurology.

For the sake of semantics and clarity of what is meant by emotion, the sublimely simple definition of Professor John R. Reid in the preface of Cobb's book is offered at this juncture: "Both the feeling and the behavior that expresses it, as well as the internal physiological responses to the stimulus-situation, constitute a dynamically interrelated whole, which is the emotion." To the neurologists, therefore, there are three phases of emotion: (*a*) the subjective private feeling, (*b*) the discharge into the visceral nervous system, and (*c*) the motor component in bodily, overt behavior.

SUBJECTIVE PHASE OF EMOTIONS

On the subjective side of emotion, animals give us too little data and humans too much or, more accurately, too much elaboration of pure, primal emotion.

Neurologists should consider the meaning and significance of the term cenesthesia, which is found more often in foreign medical treatises than it is in those of this country. Cenesthesia is the general feeling of being in the body or of bodily consciousness without reference to any part or any specific sensation. It can be said with axiomatic conviction that to be conscious of any extraneous stimulus, one must first be conscious of oneself as a total

2. Spiegel, E. A.: The Central Mechanism of Emotions, American Psychiatric Association Annual Meeting, Cincinnati, May 7-11, 1951.

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diffuse sense of merely being. Cenesthesia therefore, can be called the irreducible level of all consciousness. No outside stimulus reaches any level of consciousness unless it is infused with this element of cenesthesia.

How cenesthesia is created is or should be one of neurology's most urgent problems. Whether the homeostatic centers of the hypothalamus furnish it through their humoro-sensitive capacities rather than through afferent systems from the viscera is still an open question. Verney's [3] demonstration of osmoreceptors in the supraoptic nucleus for maintaining water balance suggests the possibility that other unique receptors participate to synthesize basic feeling tone in the hypothalamus. Destruction of the caudal portion of the hypothalamus by Bard [4] and later by Bailey and Davis [5] led to the production of mutism and akinesia, particularly of faciovocal activity. This inspired Nielsen and Thompson [6] to regard these cells about the upper aqueduct as the centers of conation and as the origin of drive to maintain all tissue optimum by infusing the organism with primal animation, feeling and crude psychic energy.

Few neurological entities in man are encountered when basic feeling or perception of emotional tone is modified by focal anatomical lesions. It is usually assumed that extraneous stimuli are not merged with cenesthetic consciousness until they reach the thalamus and, specifically, its primary receptive field, the ventral posterolateral nucleus. Lesions in this nucleus in man are not uncommon because of thrombosis of the geniculothalamic artery, and they produce the well-known syndrome of Déjerine and Roussy with its familiar disruption of sensory thresholds.

The ventral posterolateral nucleus of the human thalamus is something more than just another sensory synapse. Therefore, lesions in this area offer an interesting study of emotional disruption on the subjective side which merit more investigation than they usually get. The main difficulty is the patient's inability to express emotional experiences in terms of clear, discriminative language. As every neurologist knows, in this thalamic syndrome, light touch when applied in a dragging manner along the skin, produces an angry, permeating disagreeable sensation invoking an emotional response which ordinarily belongs to a pain stimulus. Paradoxically, a pain or deep pressure stimulus may actually produce a feeling of relative relief or pleasure. The peculiar, qualitative experiences which perfuse the entire half of the body when a non-noxious stimulus is applied, are called hyperpathias.

Ten patients studied by me have recorded their inward feelings about hyperpathia as an "inward frenzy affecting one half of the body," as an "angry feeling without good cause," as an absurd "hemiemotionalism" and as a "hemiagitation bordering on a shrieking hysteria." In all 10 patients, this hyperpathia was mild or totally absent in the trigeminal distribution.

The agitated hemiemotionalism in two patients with the thalamic syndrome could be provoked by special sensory stimuli, such as the auditory nerve. In one patient, the distress was precipitated by the sound of his wife's vacuum cleaner and in another, by the grating sound of silverware on this plate, which required the use of wooden eating utensils.

Perhaps the best elucidation of the distorted effect in the Déjerine-Roussy syndrome was offered by a most intelligent and cooperative professional man of 58 years, a judge in a district federal court, who had excellent command of English and was unique in his ability to express the finer nuances of inward feelings. The hypesthesia-hyperesthesia paradox involved his right side. He had the typical, uncomfortable reaction to light touch, which induced an "inarticulate frenzy" on the same side. When he was angered by any disconcerting psychogenic situation, this permeating, indescribable wave of distress spread from the neck to the toes of the right foot, "as if a house current of 110 volts were passed through the same side of the body." On the other hand, whenever he was taken up with some deeply sentimental and pleasant feeling, such as that provoked by the surprise visit of a favorite married daughter from California, he became acutely aware of the pleasurable emotions of the occasion as a half-body experience involving only the intact left side. He recalled such a hemiemotionalism on the pleasurable side at least a half-dozen times.

Another patient in this series amused the junior physicians with his persistent claim that in his erotic pursuits he could clearly sense the feeling of passion in only the intact half of his body, an anatomical cleavage which even included the external genitals. This was regarded as a bit of imaginative whimsy on the part of the patient until, on further inquiry, three other male subjects admitted to the same peculiar hemieroticism and two patients after right hemispherectomy reported the same "dissociation of pleasure."

These unique examples of what can be called a hemiemotionalism or hemipassion are found only in lesions of the ventral posterolateral nucleus in humans. It is believed to be due to a localized release from diencephalic and cortical control of the thalamus. From Spiegel's [7] extensive thalamotomy experiments, we know one cannot say that there is a single thalamic center of emotions. However, this nucleus does produce a distinct anatomical dissociation of feeling function and thereby furnishes one useful clue in the organic studies of emotional synthesis.

AUTONOMIC PHASE OF EMOTIONS

Adhering to Reid's definition of what constitutes an emotion, the second phase deals with the concomitant discharges in the emotional experience which take place in the visceral nervous system. This phase of emotional physiology lends itself to the easiest and most reliable objectivity. Along with the excellent pioneer investigations of Pavlov and Cannon, the mass of data available today is largely due to the enthusiasms of psychomatic medicine and is too well known and too comprehensive to allow for any comment in this strictly neurological discourse.

3. Verney, E. B.: Croonian Lecture: The Antidiuretic Hormone and the Factors which Determine its Release, Proc. Roy. Soc., London, s. B. **135**: 25, 1947.

4. Bard, P.: Emotion: The Neuro-Humoral Basis of Emotional Reactions, in Murchinson, C.: A Handbook of General Experimental Psychology, Worcester, Mass., Clark University Press, 1934, pp. 264-311.

5. Bailey, P., and Davis, E. W.: Effects of Lesions of the Periaqueductal Gray Matter in Cats and Monkeys, Arch. Neurol. & Psychiat. **53**: 325 (April) 1945.

6. Nielsen, J. M., and Thompson, G. N.: The Engrammes of Psychiatry, Springfield, Ill., Charles C Thomas, Publisher, 1947

MOTOR PHASE OF EMOTIONS

Far more intriguing are the recent advances in the study of the motor, or expressive, phases of the emotions. It is an interesting commentary that after Charles Bell [7] described amimia in 1806, after Duchenne's [8] electrical stimulations of facial expression, in 1862, and after Darwin [9] wrote his "Expression of the Emotions in Man and Animals" in 1872, there was a notable lack of interest in pursuing the study of the motor side of the emotions. This was in spite of the observations made long before by Parkinson,[10] who established a clinical entity noted for its defect in spontaneous emotional animation. Because clinicopathologic correlations in almost all types of parkinsonian rigidity are obscured by the diffuse nature of the cerebral lesions, no one could venture an exact opinion on the role of the basal ganglions in emotional expression, particularly when their direct stimulation showed these nuclei to be relatively inert.

In the modern neurophysiological concept, the function of basal nuclei in emotional expression is not denied. They are not primal centers but play an elaborating role in the so-called reverberation circuits. These are devices which allow an interplay of suppressor and facilitative mechanisms which involve the thalamus, the sensory cortex, the suppressor area 4s, the premotor and motor areas as well as the striatum and pallidum.

Another complex of structures which modify and elaborate emotional display is that proposed by Papez [11] who introduced an elaborate integration by way of the gyrus cinguli and much of what is called the rhinencephalon, all these mechanisms acting on the hypothalamus.

All these rather convincing theories about the emotions are difficult for the clinical neurologist to apply because of the elaborate and widely dispersed neural mechanisms involved. The latter somehow fail to qualify as fundamental centers of emotional expression, as primary structures for the discharge of those spontaneous, massive, postural and facial activities which are considered direct expressions of pure feeling.

Neurology has been looking for something like a "final common pathway" for emotional expression. It is a safe premise that such a mechanism is phylogenically old and will be found in a very old motor system in the brain. Bell sensed it when he drew attention to the facial muscles as the best expressers of human feeling and that the stimulus for facial expression arises from a primitive portion of the motor system. He first drew attention to the simple fact that patients can have a voluntary weakness of one angle of the mouth, but in spontaneous laughter or grimace the facial activity is complete. He also mentioned that the opposite condition can occur and therefore concluded that voluntary control and emotional control of the face arrive from different motor centers. Even in the preexperimental and purely empiric days of Darwin, the latter recognized that the emotions are discharged through phasic postural states of the body, through respiratory activation, and, in human beings, essentially through plastic activities of facial muscles.

The motor side of the emotions, then, is primarily a complicated synthesis of posture, respiration and facial activation. No structures above the hypothalamus when stimulated in the experimental animal have duplicated a complete motor emotional ensemble. Not until the stereotaxic apparatus began to probe more accurately into the reticular formation of the brain stem were there evidences of something like primary emotional expression or absence thereof. This reticular formation occupies the tegmentum of midbrain, pons and medulla and has its caudal portion in the posterior hypothalamus.

In brief, this reticular substance is functionally divided into a repressive and a facilitative system. It is this latter structure, now often referred to as a reticular activating system, which appears to promote a quick, natural, fluid-like expression of feeling with such movements as grimacing, licking, grasping, turning, progression patterns of the arms, easy and almost reflexive faciovocal activities, all of which Darwin found to be expressions of emotional tone.

Recently, Ward, McCulloch and Magoun [12] finally produced the completely deemotionalized animal when they made electrolytic lesions at the base of the tegmentum, extending from the midbrain to the lower pontine level. Along with this synthetic parkinsonian rigidity, they also reproduced the static tremor typical of the disease.

In human beings, the neurologist may occasionally encounter a lesion restricted to the brain-stem reticulum which allows fairly accurate clinicopathologic correlations. Such a lesion is usually the spongioblastoma of the reticular substance of the pons or medulla, which has not extended into tectal or ventral structures. I studied five such patients clinically. Amimia was found to be most severe in these patients and was the very first localizing symptom in two of them. Parkinsonian symptoms, such as rigidity, tremor and asynkinesia appeared in two, one an adult of 42 and another a girl of 11 years. Both were thought to have von Economo's encephalitis, although I should have known better than to expect an encephalitic parkinsonism in a child of 11. Naturally, all these patients were eventually overwhelmed by a bulbar palsy which utterly obscured the akinesia, emotional impoverishment, and postural rigidities which theoretically are caused by a destruction of the facilitative tracts in the brain-stem reticulum.

It is doubtful whether all the specific emotional patterns are fabricated in this "semifinal" common path even if we include the most caudal portions of the reticular formation and the central gray substance in the posterior hypothalamus. Stimulation of the latter structure in cats produces the rage reaction, but when the primate is subjected to the same test, the result is not the same. We must concede that it requires more than reticular substance to compound and fabricate the emotions. Consideration must be given then to the physiological and anatomical formulations of Papez, as well as to those engrams which involve the suppressor centers in

7. Bell, C.: Anatomy and Philosophy of Expression, ed. 1, New York, Collins & Company, 1806.
8. Duchenne, G. B. A.: Mécanisme de la physionomie humaine, ou Analyse électro-physiologique de l'expression des passions, 1862.
9. Darwin, C.: The Expression of the Emotions in Man and Animals, New York, Appleton-Century-Crofts Company, Inc., 1873.
10. Parkinson, J.: An Essay on the Shaking Palsy, London, Sherwood, Neely & Jones, 1817.
11. Papez, J. W.: A Proposed Mechanism of Emotion, Arch. Neurol. & Psychiat. 38: 725 (Oct.) 1937.
12. Ward, A. A., Jr.; McCulloch, W. S., and Magoun, H. W.: Production of an Alternating Tremor at Rest in Monkeys, J. Neurophysiol. 11: 317, 1948.

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the cortex and their connections with the basal nuclei, the thalamus, and hypothalamus, which are so expertly summarized in a paper by Lindsley, Schreiner and Magoun.[13]

These sporadic samplings of both experimental and clinical study do not indicate that the neurologist is ready to submit a good organic engram for the human emotions. But the data are more complete than most medical minds believe, and there is a distinct demand for a candid and careful listing of all the material now available. The neurologist must do his part in establishing the emotions as part of a physical mechanism upon which the psychologist and psychiatrist can construct their own formulations.

Even the psychologist,[14] who is usually wary of the biologist, in his most quasi-philosophical moods admits that "susceptibility to any kind of emotional arousal is in a significant way a function of the sturdiness of the (anatomical) structures that direct and regulate the life of the individual. No psychology of emotion is complete without an account of these structures."

The anatomy and physiology of the emotions must not remain in a crepuscular zone. They will be fully understood only after we have developed methods of describing and plotting the essential structures and relationships, both subjective and objective, of which the emotional mind is composed.

2020 E. 93d St.

13. Lindsley, D. B.; Schreiner, L. H., and Magoun, H. W.: An Electromyographic Study of Spasticity, J. Neurophysiol. **12**: 197, 1949.
14. MacLeod, R. B.: Religious Perspectives of College Teaching in Experimental Psychology, New Haven, Edward W. Hazen Foundation, 1951.

ARE YOU AN OTOLARYNGOLOGIST?

CHAIRMAN'S ADDRESS

James Milton Robb, M.D., Detroit

By this simple direct question is meant are you a good practitioner of laryngology, otology and rhinology? This question really does not apply to and probably will have little practical interest for the superspecialists, those men who have perfected special techniques in one or two phases of this work and have limited their practices thereto. This paper is primarily intended to call to the attention of the young man about to choose his life work the importance of the specialty, its scope, the opportunities it affords, and the pleasure of its practice and to offer a challenge to the man already traveling this high road.

These superspecialists are in truth the research men in medicine and surgery of the nose, throat, and ear. What a blessing to us! They clarify our minds as to the proper method of attack in these areas. We could not do without them, for not only do they serve for reference but they also act as spurs and stimuli to the general practitioners of otolaryngology.

The broad field is our job, broad not in the physical sense but in the complexities of this small but vital area. And it is a much more responsible job than is often thought. A thorough knowledge of the embryology, physiology, anatomy, and pathology of the nose, throat, and ear as well as of the face, mouth, and neck is required, for rightly the otolaryngologist should take care of the cysts, fistulas, and tumors of teratological origin in this field.

Otolaryngology is a specialty in its own right, an important one and should not be considered a part of any other. Sometimes a practitioner may find it necessary to combine the practice of otolaryngology and ophthalmology because of the practicability of this service to the smaller communities. We all know this is not ideal, but it must be done. And it can not be emphasized too strongly that in these cases adequate training in each specialty should be taken. Neither should be sacrificed to the advantage of the other. Whether you have chosen ophthalmology or otolaryngology or a combination of the two, the national leaders in these fields have long recognized the value of intensive training beyond the walls of colleges and universities. Home-study courses have been available for some time, and the annual classes offered by the American Academy of Ophthalmology and Otolaryngology afford the opportunity of intensive study—refresher courses that not only educate but stimulate. It is impossible for any one to keep clearly in his mind the embrylogic and anatomic relationships of this area unless he is constantly thinking, studying, scanning.

So small the area! So vast the field! Through this gateway, the nose and mouth, enter all types of infections whose foci may interfere with normal health and function in distant parts of the body. And, conversely, the membrane of the nose affords barometric readings of the storms in the general system, for upon it are recorded the results of biochemical and autonomic nervous-system changes. Thus the otolaryngologist must practice medicine, surgery, or a combination of the two.

I flatter myself that I am an otolaryngologist and have been that for more than 40 years in an urban center in the Middle West. A continuing practice from this laboratory, with more than one generation of human beings as the object of my efforts, I believe has proven the efficacy of these findings concerning the field. In the following part of the paper I will discuss a few of the more important practices of otolaryngology.

The tonsil has been the most persistent target of both lay and professional writing. Whether to operate? When to operate? How to operate? And by whom? A good tonsil, like any other good organ, should be left alone. A diseased one should be completely removed. Tonsillectomy is not a simple procedure. Its performance requires the consummate skill of a man well trained in otolaryngology because only a complete removal of the diseased tonsil, leaving an absolutely clean throat, produces the desired results. The number of secondary operations attest to this.

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Closely associated with tonsillectomy is removal of the adenoids. Adenoidectomy, usually considered a very simple procedure, is probably the most poorly done operative effort in all surgery because the area cannot be readily seen. Infectious processes may have existed for years in this spongy lymphoid tissue, with a production of sinusitis, recurrent sore throats, and a surprising amount of toxemia. In addition to good anesthesia, good light, good assistants, and good suction, instruments with which to elevate the palate and thoroughly remove the lymphoid tissue are required. We should never underestimate the possibility of infection in the nasopharynx and its results. It would be a good thing if each one in otolaryngology had to have his nose operated upon early in his career, to find out how sensitive the structures of the nose really are.

A well-done submucous resection is one of the most satisfying operations because of the relief it gives the patient, for a nose blocked day and night is an extremely uncomfortable condition. When deformity is present, in addition to the submucous resection, plastic procedures, not only to correct the deformity but also to improve the appearance and function of the nose, are included.

Cases of chronic sinusitis, with or without polypoid change, have stimulated a great deal of study, to the end that conservative procedures have been sufficient to clear up many of these conditions. However, when no good results have been obtained, we should never fail to resort to radical surgery. This has been my routine practice, but my conviction was made indisputable by my own personal experience. After a year at least of conservative effort, a right Caldwell-Luc operation with an exenteration of the right ethmoid and sphenoid gave complete results.

There has been a tendency of late to treat the passing of endotracheal tubes, bronchoscopes, and esophagoscopes as simple, requiring little training and little care. The otolaryngologist must be ever alert to the dangers of this practice. There is no place in which good training and exacting care are more vital than in peroral endoscopy. It is still a straight and rigid tube passed along soft tissues.

The larger cysts and tumors of the mouth can be handled much more easily with intratracheal anesthesia. To those who are more accustomed to working under these conditions rightfully belongs this surgery, especially of the large cysts arising from the cervical sinus. Even under the most advantageous circumstances, these cysts are not easy to excise.

The removal of teratological developments in the face, mouth, and neck are most interesting and frequently difficult surgical procedures. These teratological developments have never elicited the proper interest of otolaryngologists in spite of the fact that their origin is in the throat, whence they travel far afield into the structures of the neck. The removal of a thyroglossal cyst and tract demand careful dissection, especially if there are accessory tracts. Experience has shown that removal of the central section of the hyoid bone at the time of the operation is essential. Lateral cervical fistulas are best removed by the insertion of a filiform bougie and the use of stepladder incisions. The fistula must be completely excised from its exit in the neck to the pharynx, just back of the tonsil. The facial nerve has always been a prime interest of the otolaryngologist; therefore, the outlining of its distal branches with the removal of parotid tumors should be within his scope.

With our aging population the care of the malignancies of the nose, throat, and larynx and their extensions into the surrounding tissues present another field for serious effort. No one can tell as he attacks a malignant process in these tissues how far it has extended, and this extension, of course, must be removed along with the primary source of involvement.

In spite of the use of chemotherapy and antibiotics, we still encounter some of the serious complications of the middle ear and mastoid diseases, such as brain abscess, acute thrombophlebitis of the lateral sinus, and labyrinthitis. These conditions may become very serious because they are seldom expected. We must never close our minds to their possibility!

There is no place in the body where reactions in the general system are shown better than in the membranes of the nose and throat. These reactions are evidenced by changes in the color, moisture, secretion, and sponginess of the membrane. What the trigger mechanism is that produces these reactions is at times difficult to determine, but it must be sought by the physician in attendance. A blocked nose is not always due to a deviated septum. A wide open nose is not always due to the atrophic change associated with chronic infection. The dry throat and hoarse voice are not always due to smoking or tumor of the vocal cord. Nor is the sense of a lump in the throat always due to the thyroid adenoma, branchiogenic cyst, or cancer. Medical otolaryngology has a very wide field into which enter allergic response, dietary deficiencies, blood dyscrasias, endocrine dysfunction, sympathetic and parasympathetic imbalance, and many other entirely medical problems. It is true that we need the help of the internist, pediatrician, allergist, and specialists in other divisions of medicine, but no one can visualize the condition of the nose and throat tissue as well as we who are constantly surveying the area.

In conclusion, this specialty is an important one in its own right. Because of the complexities of the area covered by it, constant re-education in the embryology, physiology, anatomy, and pathology of the nose, throat, and ear as well as of the face, mouth, and neck is essential to good practice. Otolaryngology offers a wide range for the surgeon, a broad field for those more interested in the medical side, and unlimited horizons for the general practitioner of otolaryngology—for our horizon is but the limit of our vision.

1553 Woodward Ave.

Therapy of Ménière's Disease.—A number of operations have been developed for alleviating the intractable vertigo of Ménière's disease in those patients in whom medical therapy either has failed or the institution of such a regimen was impractical. The primary purpose of these procedures has been the prevention of the acute episodes of vertigo. The available data tend to indicate that this is most consistently accomplished by resection of the eighth nerve and avulsion or electrocoagulation of the membranous horizontal semicircular canal.—Frank D. Lathrop, M.D., Surgery of Ménière's Disease, *The Surgical Clinics of North America*, June 1951.

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CLINICAL SIGNIFICANCE OF NIPPLE DISCHARGE

Edward F. Lewison, M.D.
and
Robert G. Chambers, M.D., Baltimore

The significance of nipple discharge lies in the insignificance with which it is regarded. Cancer detection requires an accurate appraisal and interpretation of the importance of nipple discharge in diseases of the breast.

This review constitutes a statistical survey of 114 patients with nipple discharge who were operated on in the Johns Hopkins Hospital during the 10-yr. period 1940-50. All patients were hospitalized, and the validity of the diagnoses was based upon pathologic evidence obtained in the operating room by the scalpel rather than by the random probing of an aspirating trocar. The difficulties of our experience at the breast clinic have cautioned us against the peril of putting too much faith in the thin ice of diagnoses based on clinical impressions alone. Thus, we have intentionally excluded from this study all patients who were classified as outpatients and who have never had their clinical diagnoses verified by microscopic examination. Riddell [1] in his recent Hunterian lecture on carcinoma of the breast, stated that it is "wise to accept with humility that, however experienced we are, we cannot differentiate with certainty on clinical grounds alone between nonmalignant and early malignant" breast lesions.

INCIDENCE

During the 10-yr. period between 1940 and 1950 there were a total of 2,195 patients hospitalized at the Johns Hopkins Hospital for a great variety of diseases of the breast. In the classified index of diagnoses these patients were found to be grouped in 48 different categories and subcategories of breast lesions in the files of the hospital record room. Thus, from among 2,195 patients with breast disease there were 114 patients with nipple discharge—an incidence of 5.2%. Included in this group were (1) patients whose primary complaint was discharge from the nipple and (2) patients whose nipple discharge was secondary to a menacing mammary disease or perhaps incidental to hospitalization for a primary disease unrelated to the breast but subsequently necessitating breast surgery. At the time of initial examination, 74% of the patients had clinical evidence of breast disease determined by physical examination. However, 26% of the patients had no physical sign other than discharge from the nipple. Thus, no evidence of breast tumor could be detected in about one-fourth of the cases. The duration of discharge in all patients ranged widely from three days to seven years.

In a report by Hinchey [2] of all breast cases seen in the tumor clinics of the Massachusetts General Hospital and the Boston dispensary, 8.3% of 1,051 patients had nipple discharge. Many of these were outpatients, and the diagnosis could be confirmed by microscopic examination in only 78%. In a review of 2,269 cases of mammary lesions treated in the department of surgery at the State University of Iowa hospitals, Donnelly [3] found 9.6% to have discharge from the nipple. There were in this series of patients 217 females and two males. At the Johns Hopkins Hospital there was an almost identical ratio of 113 females and one male with nipple discharge. The ratio of white to Negro patients was 64 to 50, but this may reflect merely the hospital bed capacity for the segregation of the races. Also, it is well to consider that Baltimore has a white to Negro population ratio of about four to one.

PHYSIOLOGY AND PATHOLOGY OF BENIGN BREAST DISEASE

Benign breast disease is a common but perplexing condition the cause of which is obscure, the pathology puzzling and the treatment empiric and unsatisfactory. The medical literature is replete with many excellent papers, notably by Nelson,[4] Nathanson,[5] Atkins,[6] Taylor,[7] and Haagensen,[8] which tend to interpret the pathology of benign breast disease on the basis of an abnormal physiology of the breast. Since the mammary gland is often considered physiologically as a satellite of the female reproductive system, it would be expected, quite naturally, to respond to hormonal stimulation by the anterior pituitary, adrenals and gonads. The hormonal relationship of the posterior pituitary, pancreas and thyroid to the breast is vague, but not entirely unlikely. Nervous stimuli are also rather indefinitely involved in the uncertainties of breast physiology. Actual morphologic changes in the breast, however, are known to be quite closely related to various phases of the reproductive cycle.

It has been rather well established that the cyclic changes that normally occur within the breast can be correlated with the degree of estrogen and progesterone activity. Mammary gland proliferation and branching of the ducts with little or no development of the alveolar system is known to be the result of estrogenic or ovarian follicular hormone stimulation. Progesterone, in combination with estrogens, but not alone, induces extensive development of the breast to the compound acinar or alveolar stage. Whether these changes are due solely to ovarian activity alone is still speculative. Also, there is every reason to believe that variation in physiologic response may be in part due to the complex changes that

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1. Riddell, V.: Early Diagnosis and Treatment of Carcinoma of the Breast, Brit. M. J. **2**: 635, 1948.
2. Hinchey, P. R.: Nipple Discharge: Clinicopathologic Study, Ann. Surg. **113**: 341, 1941.
3. Donnelly, B. A.: Nipple Discharge, Ann. Surg. **131**: 342, 1950.
4. Nelson, W. O.: Endocrine Control of the Mammary Gland, Physiol. Rev. **16**: 488, 1936.
5. Nathanson, I. T.: Present Concepts of Benign Breast Disease, New England J. Med. **235**: 516 and 548, 1946.
6. Atkins, H. J. B.: Chronic Mastitis, Lancet **1**: 707, 1938.
7. Taylor, H. C., Jr.: Relation of Chronic Mastitis to Certain Hormones of the Ovary and Pituitary and to Coincident Gynecological Lesions, Surg., Gynec. & Obst. **62**: 129 and 562, 1936.
8. Haagensen, C. D.: The Surgical Physiology of the Breast, S. Clin. North America **29**: 1659, 1949.

consist of epithelial proliferation, cyclic growth and regressive phases, vascular and secretory alterations, and changes in the water balance of the body due to endocrine influences. Changes within the connective tissue or epithelial elements of the breast depend on the rise and fall in the number of hormones that originate principally in the gonads and to a lesser degree in the pituitary and adrenals. This response to growth stimuli or abnormal involution following a normal response is the basis for understanding the pathologic changes of benign breast disease. Yet one must bear in mind that there is a wide gradation of responsiveness to hormones that is present in both animals and man. This is true not only of more than one breast, but also of different portions of the same breast. Since the breast is not a static organ but rather a dynamic one dependent upon the action of hormones, Womack [9] has suggested that time is the fourth dimension to be considered in breast pathology—the reaction of certain target cells to certain stimuli acting over a certain period of time.

For the purpose of this paper, benign breast disease will be divided arbitrarily into three major categories, namely, (1) chronic cystic mastitis, (2) fibroadenoma and (3) papilloma. Although the term chronic cystic mastitis is a medical misnomer and catchall for a variety of painful and/or nodular lesions of the breast not due to neoplasia, inflammation, or necrosis, yet, in the matter of terminology "the chains of habit are generally too weak to be felt till they are too strong to be broken." The opinion of the profession is biased in favor of the term chronic cystic mastitis because it is accepted by all, advocated by authority, and recommended by custom. The artillery of synonyms coined to describe the histological changes associated with chronic cystic mastitis are legion. Fibrocystic disease, mastopathy, nodular hyperplasia, cyclomastopathy, Reclus' disease, Bloodgood's blue-domed cysts, Schimmelbusch's disease, mazoplasia, cystipherous epithelial hyperplasia, chronic mastitis, mammary dysplasia, mastodynia, adenosis, adenocystic disease and many other complex and hybrid names are often repeated in the literature, thus adding chronicity to the confusion.

TABLE 1.—*Incidence of Various Types of Nipple Discharge*

	Hinchey		Donnelly		Present Series	
Type of Discharge	No. of Cases	%	No. of Cases	%	No. of Cases	%
Serosanguineous	36	54	121	55	54	47.4
Serous	16	22	47	21	33	28.9
Whitish (milky)	5	7	13	6	12	9.9
Watery	2	3	..	..	8	7.0
Miscellaneous	8	13	38	17.3	7	6.8

Fibroadenomas are among the most frequent tumors that occur in young women, and are particularly common in the Negro race. They are characteristically firm and solid, may be round or lobulated, most often are freely movable and not attached to the skin or surrounding tissue and are infrequently the source of nipple discharge. Microscopically, fibroadenomas reveal an increase in connective tissue stroma with a hypertrophy of ducts and ductal epithelium. These tumors have been known to change in size and appearance during various phases of the menstrual cycle and most noticeably during pregnancy.

Chronic cystic mastitis frequently occurs in women of middle life and is often associated with premenstrual breast pain and engorgement, tenderness to palpation, nodularity that may be deceptively firm, and, less frequently, discharge from the nipple. There is often a proliferation and desquamation of the ductal epithelium with dilatation and the formation of cysts. The interstitial connective tissue is increased, and there is noted an infiltration of small round cells. Many variations and gradations of this pathologic process exist.

Particular mention should be made of a type of chronic cystic mastitis specifically characterized by discharge from the nipple. The secretion may be of any type and of any degree of viscosity. Dilatation of the ducts adjacent to the nipple or beneath the areola can usually be palpated by careful examination. Nathanson [5] suggests that this syndrome is probably due to an ovarian dysfunction resulting in incomplete involution caused by an anovulatory menstrual cycle.

Papillomas are usually associated with varying degrees of epithelial hyperplasia within the duct system of the breast. Duct cells proliferating in complex branching patterns are supported by a thin connective tissue and highly vascular core. The location of these tumors and their fragile growth structure make them particularly vulnerable to damage and resulting hemorrhage. The more marked papillomas may occur within a cyst, with or without a definite stalk deep within a duct in a breast lobule, or as a gross and readily felt papillary lesion in the subareolar region. These palpable nodules are frequently multiple and may be detected by transillumination, careful manual examination and pressure tests, and by mammography. Segmental stretching and point pressure around the areola will often result in exact localization of the source of serous or serosanguineous discharge from a papilloma. Microscopic papillomas are frequently found universally distributed throughout the breast in the presence of gross disease. Donnelly [3] notes that even with incomplete microscopic studies (the task of serial sectioning of breasts would be appalling) at least 20% of papillomas were multiple in character. Our experience corroborates the fact that invariably if papillomas are carefully sought after they will be found to be multiple and extensive.

TYPE OF NIPPLE DISCHARGE

The wide range of abnormal physiology of the breast gives scope for a great variability in the classification of nipple discharge. It is doubtful if any two hospitals, any two surgeons, or any two series of cases could be precisely proportional. Inasmuch as these proportions depend upon so many factors, it is indeed surprising that the several series reported are so closely comparable (Table 1).

The spectrum of secretion from the nipple can be of almost any color and description. Separate ducts within the same nipple and at the very same time may secrete diverse types of discharge. During the course of close clinical observation it is not uncommon to find a change in the character or color of the initial discharge from the

9. Womack, N. A.: Benign Lesions of the Breast, J. Kansas M. Soc. (Cancer Suppl.) 50: 64, 1949.

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nipple. These shades of difference, however, may be representative of quite distinct and unrelated diseases of the breast. To determine whether there was any constancy or correlation between the type of nipple discharge and a specific lesion of the breast, our figures were analyzed in Table 2. Except perhaps for papilloma there would appear to be only a haphazard relationship between the type of nipple discharge encountered and the underlying mastopathy. All cases of papilloma with nipple discharge showed the presence of either a serosanguineous or a serous secretion. Cancer and benign breast disease (a lumping category mentioned previously) are quite similar in the types of nipple discharge noted. Thus, it would appear clearly evident that no one type of nipple discharge is specific for a particular breast lesion, and conversely, both cancer and benign breast disease can give rise to diverse types of nipple discharge. Therefore, these alien signs are disappointing from the point of view of differential diagnosis.

Since the Papanicolaou smear technique has become a part of the laboratory routine of most hospitals, there have been several studies indicating its usefulness as applied to breast secretions. Material for examination is usually obtained either by direct smearing of secretions or by trocar aspiration of a suspicious area in the breast. From our very limited experience with this technique its value as a diagnostic aid will require further evidence.

Gray and Wood [10] noted, in their study of both benign and malignant papilloma of the breast, that a discharge from the nipple occurred in 77% of their 227 cases. In all of their papilloma cases, as in all of our cases, the secretion was serous or serosanguineous. In discussing the significance of a serohemorrhagic or hemorrhagic discharge from the nipple, Adair,[11] Judd,[12] and Miller and Lewis [13] found about the same proportion of benign and malignant lesions responsible for the abnormal discharge. In studying a group of cases of benign breast disease (fibrocystic disease and papilloma) Mingazzini [14] found that a sanguineous discharge was the first sign of disease in a majority of cases. In one case, discharge from the nipple preceded the development of a tumor by 10 yr. and in another case, by six years.

Among the types of nipple discharge found less commonly one notes the occasional occurrence of a whitish or milky secretion. This white discharge from the nipple may be milk, pus or carcinoma cells. A cytological examination of the secretion should insure a reliable and ready differentiation. Cheatle and Cutler [15] reported one example of a thick white discharge that consisted of carcinoma cells from a subareolar duct cancer.

Among the miscellaneous types of nipple discharge, one may find a thick greenish discharge from the nipple. This is usually the result of retained secretions following lactation, which stagnate within dilated ducts. As suggested by Geschickter [16] this inspissated or grumous discharge may become contaminated with Bacillus pyocyaneous, an infection accounting for its garish green color. Others believe that it may be due to disintegrating blood pigment. In an interesting study by Stajano,[17] of Montevideo, many different types of abnormal secretions of the breast were discussed. He called particular attention to a relatively infrequent type of gray or black secretion that is of practical importance because it may closely simulate and be mistaken for a sanguineous nipple secretion. Many phagocytic cells of the reticuloendothelial system filled with particles of melanin were present in the secretion of the patients he observed.

ETIOLOGY OF NIPPLE DISCHARGE

The careful observations of many investigators have shown that most cases of nipple discharge are caused by (1) chronic cystic mastitis and fibroadenoma, (2) papilloma, and (3) cancer. Donnelly [3] notes that chronic mastitis was responsible for 25% (55 cases) of nipple discharge in his series; intraductal papilloma was responsible for 30% (66 cases), and cancer, including Paget's disease, was responsible for the remaining 45% (98 cases). Hinchey [2] found that proliferative cystic disease and hormonal dysfunction caused 54% (36 cases); intraductal papilloma 10.5% (7 cases), and cancer, including Paget's disease, 36% (24 cases) of discharge from the nipple. In limiting this study to the bleeding nipple alone Campbell [18] recorded the following sources of discharge: cystic disease 24% (13 cases); papillomas 36% (19 cases), and cancer 38% (21 cases). Arthur Purdy Stout,[19] a surgical pathologist particularly skilled in the pathology and nosology of breast lesions, finds the foregoing facts and figures refutable. He is "astonished to find that . . . there are still physicians who believe that in more than half of the women showing this sign (bleeding from the nipple), the cause is cancer. This is, of course, entirely contrary to the facts."

TABLE 2.—*Relation of Breast Disease to Type of Discharge from the Nipple*

Type of Discharge	No. of Cases			
	Chronic Cystic Mastitis and Fibroadenoma	Papilloma	Cancer	Total
Serosanguineous	21	25	8	54
Serous	24	2	7	33
Whitish (milky)	11	0	1	12
Watery	3	0	5	8
Miscellaneous	6	0	1	7

Nonetheless, from an analysis of the data generally available, benign breast lesions accounted for about

10. Gray, H. K., and Wood, G. A.: The Significance of Mammary Discharge in Cases of Papilloma of the Breast: Clinical and Pathologic Study, Arch. Surg. **42**: 203 (Feb.) 1941.

11. Adair, F. E.: Sanguineous Discharge from the Nipple and Its Significance and Relation to Cancer of the Breast, Ann. Surg. **91**: 197, 1913.

12. Judd, E. S.: Papilloma of the Breast, Journal-Lancet **37**: 141, 1917.

13. Miller, E. M., and Lewis, D.: Significance of a Serohemorrhagic or Hemorrhagic Discharge from the Nipple, J. A. M. A. **81**: 1651 (Nov. 17) 1923.

14. Mingazzini, I.: Seilla etiologia e sul valore clinico dello scolo di sangue del capezzolo della mammella, Arch. ital di chir. **50**: 165, 1939.

15. Cheatle, G. L., and Cutler, M.: Tumours of the Breast: Their Pathology, Symptoms, Diagnosis and Treatment, Philadelphia, J. B. Lippincott Company, 1931.

16. Geschickter, C. F.: Diseases of the Breast, Philadelphia, J. B. Lippincott Company, 1948.

17. Stajano, C.: La seudo-mama sangrante: Las secreciones pigmentarias pardas o verdes del seno simulando la secreción hemática: Criterio diagnóstica, pronóstica y terapéutico, An. Fac. de med. de Montevideo **26**: 243, 1941.

18. Campbell, O. J.: The Bleeding Nipple, Surgery **19**: 40, 1946.

19. Stout, A. T.: The Role of Pathology in Lesions of the Breast, South. M. J. **43**: 208, 1950.

60% of the cases of nipple discharge, and malignant lesions, about 40%. In the present group of Johns Hopkins Hospital cases (Table 3) benign lesions of the breast were the source of almost 80% of the cases of nipple discharge, whereas malignant lesions were the source of only 20% of these cases. It is not an altogether surprising measure of merit to find a high index of suspicion associated with a low incidence of cancer among the patients with breast disease who reach the operating room. For no case is as early as it seems and "We must grow more and more accustomed to suspecting malignant disease on less and less clinical evidence." [1]

Careful examination of Table 3 confirms the impression that many diseases of the breast may be the source of secretion from the nipple. In addition to the causes

TABLE 3.—*Lesions of the Breast Causing Nipple Discharge in 114 Patients*

	No. of Patients	%
Benign breast disease		
Chronic cystic mastitis *	46	40.3
Chronic cystic mastitis with abscess and inflammation	6	5.3
Chronic cystic mastitis with galactocele	2	1.7
Fibroadenoma	11	9.7
Papilloma	27	23.7
Total	92	80.7
Malignant breast disease		
Carcinoma	13	11.2
Paget's disease	9	8.1
Total	22	19.3

* An all-inclusive catchall for a variety of benign breast lesions associated with chronic cystic mastitis.

TABLE 4.—*Surgical Treatment of 114 Patients with Discharge from the Nipple*

	No. of Patients		
Lesion	Biopsy or Local Excision	Simple Mastectomy	Radical Mastectomy
Chronic cystic mastitis	32	20	2
Fibroadenoma	9	2	0
Papilloma	17	10	0
Paget's disease	1 *	4	4
Cancer	0	0	13

* This patient refused further treatment.

listed in Table 3 Adair [11] noted that seven out of 10 patients with plasma cell mastitis had a nipple discharge. Specific and nonspecific ductal diseases are often associated with nipple discharge. An endocrine factor has been suggested as the etiological basis for some cases, although most investigators have been unable to confirm this by means of the urinary hormone assays available at present. The measurement of steroid biologic waste products in the urine is often a routine ritual responsible for one's bewildering oneself scientifically. Perhaps the key to the problem of effective hormone estimation should be sought in efficient methods of blood level determinations rather than in urinary assays. Whether new and more precise yardsticks and blood tests will confirm this point of view remains to be seen. In our group of 114 cases 7% (8 cases) gave quasi-clinical or laboratory evidence of hormone imbalance. A whitish discharge was present in two, and a serous discharge was present in six, of these cases. Gynecomastia in a young male was the source of a milky discharge in one of the above cases. Trauma was associated with nipple discharge in only 4.4% (5 cases).

20. Bloodgood, J. C.: Benign Lesions of Female Breast for Which Operation Is Not Indicated, J. A. M. A. **78**: 859 (March 25) 1922.

21. Slaughter, D. P., and Peterson, L. W.: Indications for Simple Mastectomy, Surg., Gynec. & Obst. **85**: 456, 1947.

TREATMENT

A review of the surgical press reveals a disconcerting lack of uniformity in the treatment of patients with discharge from the nipple. Although the subject has prompted a free and diverse discussion in the contemporary as well as in the time-honored annals of medical literature, the significance and therapy of nipple discharge remains independently in keeping with the custom of each individual surgeon. In the etiology and pathology of underlying breast disease, our clinical experience is long but our basic knowledge is short. This serves variably as a beacon to some and a scarecrow to others. It is unfortunate but true that observational pathology has been unable to pigeonhole all breast diseases into error-tight compartments of benign and malignant lesions. Thus, the deliberation and decisions required in treatment of patients with nipple discharge are too often based on ill-defined and intangible clinical judgment.

Bloodgood,[20] a renowned authority of great influence in the evaluation of diseases of the breast, was strongly prejudiced regarding the lack of significance of discharge from the nipple as a diagnostic sign. From among his voluminous contributions one may quote the following:

> Discharge from the nipple, like pain, is not an indication of a lesion of the breast for which operation is indicated. . . . There is no evidence that these lesions are precancerous, and the prevailing view that a woman with a discharge from the nipple should be protected from cancer by the removal of the breast is based on fear and not on fact.

The conservative convictions of Campbell [18] indicate that "too much fear, even panic, has been exhibited toward the symptom of bloody discharge from the nipple." In accord with Campbell are Slaughter and Peterson [21] who believe that "the diagnosis of 'chronic cystic mastitis,' the presence of a bleeding nipple, or of intraductal papillomas without cellular atypism, do not indicate a prophylactic simple amputation, especially in young women." In a small series of patients with bleeding from the nipple but without a palpable tumor, Saltzstein and Pollack were not impressed by the potentially malignant nature of the condition. Local excision in preference to "prophylactic" simple mastectomy was performed in six of the seven patients operated on. Follow-up studies, however, are not recorded. Geschickter,[16] a disciple of Bloodgood, reviews the pros and cons of nipple discharge as a sign of mammary lesions and concludes "proper investigation of the symptom is of the utmost importance." Gray and Wood [19] of the Mayo Clinic present the results of their clinical and pathologic study and "emphasize particularly the fact that discharge from the nipple, of any nature whatsoever, was found to be of great significance." To those who seek comfort in hope rather than in experience Gray and Wood offer the warning "that in 48% of our series of patients with

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malignant papillomas no tumor was demonstrable. No tumors were palpable in 60% of all patients with malignant papillomas who had experienced discharge from the nipple." In general, Donnelly [3] favored more active surgical treatment for patients with nipple discharge.

Of the 219 patients treated at this hospital, 36 or 17 per cent did not have a palpable mass when examined. All but one of these patients were operated upon, and the type of lesions found on histologic examination are of definite interest, in that thirty of the lesions showed definite evidence of hyperplasia. Five patients had malignant lesions. Six patients had lesions showing definite precancerous change.

In the present series of 114 patients with nipple discharge Table 4 indicates that there was a variable standard of surgical treatment. Most patients who were considered to have chronic cystic mastitis on the basis of frozen section were treated conservatively by a simple local excision. When the lesion was widespread with diffuse nodularity or when there were marked hyperplastic changes, with or without the presence of a distinct tumor, simple mastectomy was the treatment of choice. In two patients radical mastectomy was performed because the frozen section was reported to be carcinomatous; permanent sections failed to confirm this diagnosis. Most patients with fibroadenoma were treated by local excision. The treatment of papillomas was distinctive and individualized for each particular patient. Whenever the histological changes were multiple and showed evidence of diffuse hyperplasia, simple mastectomy was favored in preference to local surgery.

Paget's disease is a breast cancer arising in the epidermoid structures of the nipple and areola. Although radical mastectomy is the treatment of choice, it was performed in only four out of nine patients. One patient steadfastly refused to have any type of operative procedure beyond a local excision. All other patients with breast cancer were treated by radical mastectomy.

COMMENT

Nipple discharge is a sign of abnormality within the breast. Despite the difficulties of differential diagnosis presented by this sign, it can be assumed that secretion from the nipple betrays an early and unsuspected ductal or ductal-acinar disease. If one could be certain that the relationship between benign breast disease and cancer is merely one of chance association rather than of elusive cause and effect, one could perhaps strongly defend endocrine therapy as the treatment of choice in restoring an abnormal breast physiology. However, in the present series there were 22 cases of cancer of the breast with discharge from the nipple. In 14 (64%) of these cases there was an associated history of benign breast disease. There is an imperative need for a more careful analysis and evaluation of the relationship between benign breast disease and cancer. The argument for this type of study lies in the weakness of our present methods of treatment.

No attempt at a long-term follow-up could be made in this short-range investigation. However, in our study there were 63 patients with benign breast disease who were followed up for varying periods of time from one to 10 yr. Regardless of the surgical procedure performed, breast cancer did not develop in any of these patients during their brief period of follow-up observation. It would be of great importance to know whether these patients with manifest benign breast disease can look forward to a future free of danger.

Of 104 patients with chronic cystic mastitis, Donnelly [3] was able to obtain a postoperative follow-up study on 61. It is significant to note that those patients who subsequently had difficulty were those treated by local excision. Among others with precancerous lesions, six patients treated conservatively by means of simple excision alone ultimately developed cancer. Every example of a recurrent malignancy in patients receiving inadequate surgery strengthens the argument for ample exploratory operations on the breast.

SUMMARY AND CONCLUSIONS

This study constitutes a report on 114 patients with nipple discharge. The incidence of this clinical sign in 2,195 patients with variegated breast disease was 5.2%.

Benign breast disease, which includes chronic cystic mastitis, fibroadenoma and papilloma, was the source of about 80% of the cases of nipple discharge, whereas malignant breast disease, which includes Paget's disease, was the source of 20% of the cases. No sign of a palpable breast tumor could be found in 26% of either benign or malignant cases.

The evidence indicates that no one type of nipple discharge is specific for a particular type of breast lesion, and conversely, cancer as well as benign breast disease can give rise to diverse types of nipple discharge. However, in all cases of papilloma there was either a serous or a serosanguineous secretion from the nipple.

Indications for surgical treatment are suggested. The onus of responsibility rests heavily upon those who pursue the policy of watchful waiting.

"We must grow more and more accustomed to suspecting malignant disease on less and less clinical evidence." [1] Thus, the virtue of nipple discharge as a diagnostic sign in foresight may be irretrievably lost in hindsight.

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Polycystic Renal Disease.—The disease may be almost silent, the symptoms causing the individual to seek medical aid being those of a medical nature and pointing to chronic uremic or hypertensive states. The complaints may be of loss of weight, digestive disturbances, dizziness, headaches, malaise, or edema. In some instances, an abdominal mass may have been noted by the person himself with no other difficulty being experienced. More frequently, there will be complaints of pain, or a history of hematuria with or without pain, and recurrent febrile episodes with or without urinary symptoms. The pain may be a dull, chronic, ill defined lumbar ache. In many instances, there are superimposed recurrent attacks of sharp pain, typical of renal colic. It has been theorized that the dull nagging pain may be due to traction on the renal pedicle by the enlarged heavy kidney. The sudden sharp colicky pain may be due to sudden overdistention or rupture of the cysts by hemorrhage into the lumen. If there is gross hematuria with passage of clots, these may cause typical ureteral colic. The hematuria may be recurrent and painless or with colic as noted. In some instances the hemorrhage may be so severe and persistent that surgical measures, even nephrectomy, may be required for its control.—Frank N. Buck, R. Carl Bunts, and Austin I. Dodson: Preservation of Renal Function in Polycystic Disease, *The Journal of Urology*, July, 1951.

PREVENTION OF EMBOLIC COMPLICATIONS FROM VENOUS THROMBOSIS AFTER SURGERY

STANDARDIZED REGIMEN OF EARLY AMBULATION

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and
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Recently published reports demonstrate that the great amount of work done during the last decade in experimental and clinical investigations on thrombo-embolic complications after surgical operations, particularly in relation to the use of anticoagulants and venous ligation, has not solved the problem from a practical clinical standpoint. In our experience, venous thrombosis is not necessarily a serious postoperative complication when treated aggressively by early ambulation. It seems imperative to reemphasize the satisfactory results and the dominant role of early ambulation, when vigorously and properly employed, in the prevention of thrombo-embolic complications. The need for such emphasis, from the practical standpoint, is indicated by the fact that several institutions recently reported an actual increase in the incidence of thrombo-embolism.[1]

REVIEW OF THE LITERATURE

The experience of many surgeons and the numerous reports in the literature (Allen,[2] DeBakey,[3] de Takats and Fowler,[4] Duff and Shull,[5] Szilagyi and Alsop,[6] and a recent symposium [7] would seem, in our opinion, to make it evident that neither venous ligation nor the use of anticoagulants can solve the problem of treatment or prophylaxis of thrombo-embolism, even though both may have a limited usefulness in selected cases. Use of either of these procedures introduces numerous technical problems and requires special experience and laboratory facilities not universally available. Application of either of these procedures also introduces new risks into the situation.

Numerous instances have been reported in which fatal pulmonary emboli have occurred after ligation, from a new thrombus proximal to the point of ligation or from the opposite limb. Severe hemorrhagic complications may result from the use of bishydroxycoumarin (dicumarol[8]), and 23 deaths from this cause have been reported.[5] It is fair to assume that many times that number probably have not been described in the literature. In experiments on animals, Rogers, Barrett, and Lam [8] observed that moderate doses of bishydroxycoumarin induced hypoprothrombinemia, and did not significantly reduce the incidence of thrombosis. To be effective in reducing or preventing thrombosis, bishydroxycoumarin had to be given in quantities large enough to maintain the prothrombin level below 3%, and at that level there was also an impressive increase in hemorrhagic complications.

Since ligation of the femoral veins and the use of anticoagulants have definite therapeutic limitations and disadvantages, and prophylactically are not entirely successful nor without danger, it might be well to reevaluate the physiological approach when applied by a standardized regimen of early ambulation and leg exercises. These exercises greatly increase the velocity of the rate of blood flow in the respective veins, and prevent loosely attached clots from developing in the veins of the lower extremities and pelvis. In our experience, ambulation and leg exercises have eliminated the problem of pulmonary emboli, at least clinically. This has been widely confirmed by other authors who have reported a great decrease or absence of pulmonary embolism in surgical cases when early ambulation was employed (Lillie and others,[9] Meyer and others,[10] Nelson,[11] Shapiro,[12] Thompson and others,[13] Trice,[14] Blain,[15] Hunter and others [16]). Numerous authors state, conversely, that early ambulation has not favorably influenced the incidence of thrombo-embolic disease (Ochsner and others,[18] Powers,[17] Judd,[18] Wigginton and others,[1c] Blodgett [19]).

The reason for this disparity of opinion as to the efficacy of early ambulation and leg exercises in the prevention of thrombo-embolic complications becomes quite evident on careful analysis of the published reports. The time of initiating activity after operation, and the form and extent of exercise demanded of the patient, differ considerably among surgeons, some of whom follow a policy of "appeasement" instead of "aggression" in its administration. These differences in procedure and technique make it impossible to make strict comparisons in the various series. The impression gained from the literature, however, is that those who have achieved the best results in the prevention of vascular complications are those who initiate ambulation most promptly and require relatively vigorous and frequent exercise during the immediate postoperative period. Several authors who have reported no decrease or an actual increase in the

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incidence of thrombo-embolic disease use early ambulation and leg exercises, but do not define the term, nor do they describe their actual regimen.[20] Blodgett,[19] who reported that the incidence of thrombophlebitis was essentially the same among early risers as in a control series of patients confined to bed after operation (2.0 and 1.9%, respectively), makes no comparison as to embolism, with which we are chiefly concerned. He applies early ambulation in a much more conservative manner than we do.

ABUSE OF EARLY AMBULATION

Current reports, then, suggest that until the physiological method of postoperative care, including early ambulation and leg exercises, is more adequately standardized, and until an impressive volume of cases subjected to such a standardized regimen can be accumulated and carefully analyzed as to embolic complications, it is entirely premature and unjustifiable to assert that the incidence of embolism is not favorably influenced by this procedure. From our own experience and from conversations with surgeons and publications on the subject, we are convinced that when the results of early ambulation in preventing embolic complications after surgery are not favorable, the fault lies in abuse of this method. Abuse of early ambulation universally consists in "too little and too late" with respect to exercise.

To have the patient dangle the feet over the edge of the bed or to sit in a chair is not early ambulation. To get the patient out of bed for the first time 24 to 48 hr. after operation, and thereafter only once or twice a day is not early ambulation based on an understanding of physiological principles. To leave the decision regarding the time of getting out of bed and the amount of activity to the patient's wishes also is not early ambulation, according to our viewpoint. To allow a nursing staff not specifically instructed in the technique and rationale of early ambulation to regulate the procedure is another deterrent to effective results.

STANDARDIZED REGIMEN OF EARLY AMBULATION

In a standardized regimen of early ambulation, it is the surgeon's responsibility to order the time, frequency, and amount of ambulation and of leg exercises that are to be carried out by the patient. It is also the surgeon's responsibility to see that the nursing staff is carefully and specifically instructed [21] in the physiological principles and technique of managing these patients. It is a further responsibility of the surgeon to supervise the nursing staff in order to see that there is no laxity in demanding the maximal amount of exercise. The surgeon must not only suggest and advise that the patients get out of bed at the earliest possible moment after recovery from the anesthetic, and at regular, frequent intervals thereafter, but he must insist on this with all the authority at his command. This includes warning the patient about the risks and dangers of the development of loose blood clots in the veins of the legs, and offering calm, convincing reassurance that the exercises demanded will preclude such complications and also make him "feel better faster."

Even though the regimen that we use has been described previously in detail,[22] it seems necessary to repeat its salient features here, because our experience has proved that, to be most effective, early ambulation must be carried out vigorously and essentially as follows.

1. As soon as the patient recovers from the anesthetic, ambulation is begun, regardless of the magnitude of the operation. The contraindications to this procedure are extremely few: profound shock when the patient is practically pulseless; severe, uncontrolled hemorrhage; thyroid crisis, and in the final stage of a hopeless cancer or other disease, when death is imminent. At least four or more periods of walking are required on the day of operation. Ambulation is most important and of greatest value in patients who have been subjected to extensive surgical procedures, because here the dangerous reactions to trauma, which have to be counteracted by exercise, are severest. Prostration may limit the activity to only two or three steps on the first out-of-bed period, but experience has proved that the walking distance can be increased rapidly during each succeeding episode. By the end of the day of operation, our patients usually are able to walk a considerable distance. At first, the patient walks only a short distance from the bed, but repeats this, to and fro, on each out-of-bed period until the limit of tolerance is reached. It should be emphasized that, no matter how great the urging by surgeons and nurses, patients will not overdo. Constant reminders and orders to be more active are necessary, if the patients are to derive optimal benefit. Occasionally syncope occurs during the first out-of-bed period, but this happens far less frequently than it did when patients were confined for 10 or 15 days before they got out of bed. Syncope is usually due to fear, and can be lessened by a positive, reassuring approach on the part of the nurse or surgeon. An excellent way to rid the patient of such fear is to tell him to bend over and try to touch the floor. Repetition of this exercise a few times increases the circulation to the brain and gives the patient confidence. If syncope does occur, the patient is returned to bed immediately, but within a few minutes the procedure is repeated.

9. Lillie, R. H.; Buxton, R. W., and Duff, I. F.: Prevention and Management of Thromboembolism, Arch. Surg. **59**: 609-632 (Sept.) 1949.
10. Meyer, K. A.; Kozoll, D. D., and Capos, N.: Early Ambulation: Clinical Results and Prerequisites, Minnesota Med. **31**: 882-891 (Aug.) 1948.
11. Nelson, G. G.: Some Phases of Postoperative Care in Gallbladder Surgery, Ohio M. J. **45**: 237-240 (March) 1949.
12. Shapiro, H. P.: Early Ambulation in Postoperative Patients, Ohio M. J. **45**: 136-137 (Feb.) 1949.
13. Thompson, J. B.; MacLean, K. F., and Coller, F. A.: The Role of Transverse Abdominal Incision and Early Ambulation in the Reduction of Postoperative Complications, Arch. Surg. **59**: 1267-1277 (Dec.) 1949.
14. Trice, E. T.: Early Ambulation After Surgery, Am. J. Surg. **78**: 486-499 (Oct.) 1949; Early Ambulation as an Aid in Postoperative Management, South. M. J. **43**: 475-480 (June) 1950.
15. Blain, A. W.: Early Ambulation, J. Internat. Coll. Surgeons **9**: 568-570 (Sept.-Oct.) 1946.
16. Hunter, K. C.; Krygier, J. J.; Kennedy, J. C., and Sneeden, V. D.: Etiology and Prevention of Thrombosis of the Deep Leg Veins: A Study of 400 Cases, Surgery **17**: 178-190 (Feb.) 1945.
17. Powers, J. H.: Prompt Postoperative Activity After Hernioplasty: Its Influence on the Incidence or Complications and Rate of Recurrence, Arch. Surg. **59**: 601-608 (Sept.) 1949.
18. Judd, E. S., Jr.: Early Ambulation in Postoperative Care, Collect. Papers Mayo Clin. and Mayo Found. (1947) **39**: 777-780, 1948.
19. Blodgett, J. B.: Early Ambulation Following Surgical Procedures, Bull. New York Acad. Med. **25**: 176-184 (March) 1949.
20. Ochsner,[14] Wigginton,[16] Judd.[18]
21. In our experience, nurses are eager to learn the principles underlying physiological care of surgical patients. The film prepared by the senior author has been in almost constant circulation among nursing schools and groups, and numerous talks to nurses have been requested by hospitals and nursing organizations.
22. Leithauser, D. J.: Early Ambulation and Related Procedures in Surgical Management, Springfield, Ill., Charles C Thomas, 1946.

The following case history, of a patient who was so ill that postoperative complications, or even death, might have been expected, illustrates our aggressive approach in the use of early ambulation.

ILLUSTRATIVE CASE.—A woman, aged 53, had been ill for four days with midabdominal pain and cramps. There had been no vomiting and no evacuation of the bowels. On admission, since she was semicomatose and incoherent because of toxemia, it was impossible to obtain an adequate history from her. Her temperature on admission was 101 F. and the pulse rate was 140.

Physical examination revealed no abnormalities except dehydration, abdominal distention, Grade III, and generalized tenderness, severer in the lower abdomen and extreme in the pelvis on bimanual vaginal examination. The clinical impression was ruptured pelvic appendix, gangrenous intestines, or twisted pedicle of the ovary.

After proper preparation, a lower midline incision revealed about 6 oz. (180 gm.) of free pus in the pelvis from a large rupture of a gangrenous appendix; this was not walled off. The pus was aspirated and the appendix removed, and the abdomen was closed without a drain. After the operation, the patient remained in a semicomatose state and had to be restrained for about 10 days. Antibiotics were employed to the limit of tolerance, and fluids were administered parenterally. The temperature and pulse varied between 101 and 103 F., and 110 and 150, respectively.

On the day of operation, the patient walked with support, four times. The next five days she walked a distance of about 200 ft. (about 609 m.) in the hall four times each day. Though this patient was semicomatose and confused, she could walk considerable distances with the aid of two nurses who were well trained in the ambulatory procedure. After the sixth day, weakness limited ambulation to about 50 ft. (about 152 m.) four times each day. No food was tolerated until the 16th day, after which the walking distance was again increased. The first bowel evacuation also occurred on the 16th day. No enemas were given.

By the 18th day the patient was so much improved that she was able to walk increasing distances alone. She left the hospital, completely recovered, on the 27th postoperative day.

2. During the rest period in bed, leg exercises, as already described, are directed by means of an exercise chart, which is kept in constant view of the patient. These exercises are performed every 10 or 15 min. and it is the duty of the attending nurse to check frequently to see that they are being done properly. We feel that these exercises are extremely important, particularly on the day of operation, as an adjuvant in the prevention of loose clot formation in the deep veins of the legs.

3. During the first stages after operation, the patient is not permitted to sit in a chair. The patient walks as much as possible and then returns to bed. Until ambulation is well established and the patient is almost normally active, the patient is not allowed to sit in a chair, except for very short periods while eating a meal or while the bed is being changed. In patients who have been subjected to extensive surgical procedures, this may require several days. Even when the patient is allowed to sit in a chair, this should not be done for long periods. The bed is kept flat at all times, back rests are not permitted, and patients are never allowed to have pillows placed under their knees. We believe that the common practice of permitting patients to sit in a chair instead of walking during the early postoperative period accounts for some of the unfavorable reports.

4. During the first period out of bed, the patient is required to cough while the nurse checks for the presence of palpable rales. If rales are present, and the amount of mucus is large, vigorous voluntary coughing is required until the mucus is entirely expelled. Excessive mucus and palpable rales can be and always should be eliminated by this means. If there should be any threat of atelectasis, coughing exercises, in the standing position, are performed every two hours or oftener to obviate this danger. The patient must be encouraged to cough vigorously, for the more effort expended by the patient, the greater the benefit.

5. Only rarely is a narcotic given until after the patient has been out of bed to walk for the first time. Sedatives are employed sparingly throughout the postoperative period. In many cases they are not necessary at all. Antibiotics are employed prophylactically when indicated.

6. Electrolyte and water balance is carefully maintained during the preoperative and postoperative periods.

7. Many patients are permitted a full diet immediately after operation, usually regulated by the patient's appetite. Cathartics or enemas are not given postoperatively; they are considered dangerous in many instances. The need for use of a bedpan is extremely rare, since patients walk to the bathroom from the beginning.

8. There is no danger of wound disruption from ambulation if proper incisions and proper suture technique are used.[22]

9. It is important that, before operation, patients should be ambulatory. If, for some extraordinary reason, this is impossible, leg exercises in bed—vigorous flexion and extension of the toes, ankles, and knees at least four times every hour— should be substituted. The regimen used after surgery is merely physiological management, and it is a mistake to call it rehabilitation. If the patient's condition is such that he needs rehabilitation, it is done before operation excepting in the most acute emergency.

When the preoperative and postoperative care of surgical patients is carried out with aggressive insistence in this manner, our experience furnishes convincing evidence that the hazards of prolonged disability or loss of life from embolic complications should be practically eliminated.

THROMBOPHLEBITIS

In a series of 3,371 surgical cases, 90% of which were abdominal operations, and at least 1,631 represented so-called major surgery entailing greater hazard of embolic complication, there was no instance of pulmonary embolism either fatal or nonfatal (Table). The series does not include five cases of thrombophlebitis, the management of which deserves comment.

Two of the cases of thrombophlebitis occurred early in the series and have been previously reported.[22] Three additional instances have been observed during the past five years. One of these patients was a man who left the hospital two days after a right herniorrhaphy, completely ambulatory. On the fifth day after operation, some pain and slight swelling of the right leg appeared. An elastic bandage was applied at the time and the patient remained ambulatory, returning to our office every few days for observation. The condition improved steadily, and at the end of three weeks all pain and swelling had completely disappeared and the patient has remained entirely well. The second patient was a woman with pelvic inflammatory disease with multiple chronic abscesses (frozen pelvis). She was ambulatory immediately after

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recovery from the anesthetic, and left the hospital on the fifth day after operation. On the 18th postoperative day, there was a slight swelling of the left calf and some pain on walking. A bandage was applied and normal ambulation was continued, with the patient coming to the office for observation at frequent intervals. The pain disappeared in about 10 days, and after three months there was no residual swelling. A woman who had an abdominoperineal resection had some swelling, with no significant pain, of the left leg five days after operation. A bandage was applied and vigorous activity was continued. When the patient came to the office 10 days later,

*Total Cases Subjected to Early Ambulation to Dec. 1, 1950**

Major Procedures (prone to be complicated by postoperatalve thrombo-embolic disease)	
Gastrectomy	53
Gastro-enterostomy	14
Vagotomy (14 with gastro-enterostomy)	36
Duodenal diverticulectomy	4
Repair of perforated duodenal or gastric ulcer	16
Colon resections (anterior; right colon; obstructive, and abdominoperineal)	46
Intestinal obstruction (correction of or resection)	41
Cholecystectomy (56 with common-duct exploration)	306
Choledochostomy (gallbladder previously removed)	15
Cholecystostomy (in the aged or in extremely ill patients)	11
Choledoduodenostomy	4
Splenectomy	5
Pancreatic cyst; marsupialization	2
Kidney operations (nephrectomy; lithotomy)	18
Prostatectomy	3
Radical mastectomy	37
Hysterectomy (with and without other surgery)	148
Other operations on the female pelvis	122
Herniorrhaphy (diaphragmatic hernia)	5
Herniorrhaphy (inguinal hernia: 59 bilateral; 17 strangulated)	356
Herniorrhaphy (incisional)	41
Appendectomy (for fulminating or gangrenous appendicitis, or empyema)	312
Appendectomy (for ruptured appendix with spreading peritonitis)	35
Lumbar sympathectomy	1
	1,631
Less Hazardous Procedures (mainly abdominal surgery)	
Including exploratory laparotory; interval appendectomy for mildly acute appendicitis; femoral herniorrhaphy; umbilical herniorrhaphy; colostomy; perineal operations; rectal operations; pilonidal cyst; thyroidectomy, and all other cases remaining in the hospital over 36 hr	1,740
Total	3,371

* This includes some cases operated on by the junior authors on the surgical service of D. J. Leithauser at St. Joseph's Mercy Hospital, Detroit.

the swelling of the leg had completely disappeared and she has had no further difficulty.

Early ambulation cannot eliminate the possibility of phlebitis (inflammation), but will prevent the development of a large, loosely attached clot by greatly increasing the velocity of the blood stream. Loose clots are thus washed away when they are incipient and still in the sludge state. We have not, in the 12 years during which early ambulation has been practiced, seen a single patient with fatal or nonfatal pulmonary embolism. Venous ligation has never been used and no patient has ever received medical treatment with anticoagulants.

COMMENT

The rationale of early ambulation and frequent leg exercise has previously been described,[23] and has also been emphasized by others. It has been established that blood sludge, minute sticky clumps of red cells, are present after every surgical procedure [24] owing to the increased coagulability of the blood, and that the recumbent position results in mechanical stagnation of the venous flow.[25] Hence it follows that vigorous flexion and extension of the toes, ankles and knees (in-bed exercises), and frequent walking in as brisk a manner as possible will quicken the circulation in the veins and keep the sticky sludge moving. Thus, any loosely attached minute thrombus will be dislodged before the formation of a clot of sufficient size to cause fatal pulmonary embolism.

In discussing early ambulation with many surgeons, in visiting university and private hospitals, and in reviewing published reports, it is evident that almost none of them approach the problem in the aggressive and standardized way that has proved efficacious in preventing thrombo-embolism in our patients. Therefore, it seems to us that until those who still doubt the prophylactic value of early ambulation have applied it with this determined attitude and careful regimen in a large series of cases, this procedure, which is universally applicable in practically all surgical cases, should not be discredited by less favorable results reported by those who have used it half-heartedly and timidly, and without a completely standardized technique.

A standardized regimen embracing an aggressive attitude toward early ambulation and specific leg exercises has solved the problem of embolic complications after surgery for us. Those who profess to use early ambulation and yet continue to report cases of fatal pulmonary embolism caused by postoperative development of a thrombus in the deep veins of the leg should reexamine and reevaluate their technique of postoperative care.

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25. Baker, E. C.: Clinical and Roentgenographic Evaluation of Venography Based on Experience in 1,027 Cases, Am. J. Roentgenol. **58**: 603-616 (Nov.) 1947.

Zoonoses.—There are over 80 known diseases which can be transmitted to man by vertebrate animals. One need only cite tuberculosis, brucellosis, rabies, Q fever, and anthrax to give an idea of the importance of some of these diseases. . . . Requests for technical advice received by WHO and by the United Nations Food and Agricultural Organization (FAO) led to the setting-up of a Joint WHO/FAO Expert Group on Zoonoses, which held its first session in Geneva from Dec. 11-16, 1950. The report on this meeting has recently been published as World Health Organization: Technical Report Series, No. 40. . . . During this session the group dealt with the question of whether to formulate international sanitary regulations to reduce the risk of spreading zoonoses. . . . Is it possible to establish sanitary regulations to prevent the spread of the zoonoses, similar to the regulations dealing with contagious diseases in man? The group discussed this question, and it became evident that it would be difficult to frame regulations acceptable to all countries; for, while certain countries might be ready to impose the most stringent regulations, others would be unable to do so for economic reasons or because they are obliged to import livestock. Nevertheless, the problem is worthy of further consideration. —Diseases Transmitted to Man by Animals, *Chronicle of the World Health Organization*, May, 1951.

PATHOGENESIS OF LIVER CIRRHOSIS IN SCHISTOSOMIASIS

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One of the most important of parasitic diseases is caused by the blood fluke, Schistosoma haematobium. The disease is prevalent in North and South Africa, especially in Egypt, but also in the Sudan, Ethiopia, the Congo, and Rhodesia, as well as in Arabia, Persia, the west coast of India, Madagascar, Puerto Rico, and occasionally in Australia and the United States. Cirrhosis of the liver is among the disabilities which are caused by or are associated with the presence of this parasite. In Egypt there is a variety of cirrhosis which is attended by the presence of the ova of Bilharzia. The lesion is characterized by enormous thickening of the periportal connective tissue and is sometimes called pipe stem cirrhosis. In China and Japan and in the Philippines there is a disease known as Asiatic schistosomiasis, which is characterized by cirrhosis of the liver, splenomegaly, ascites, dysentery, progressive anemia, and sometimes focalized epilepsy. The disease occurs extensively in one district of Japan, where it is designated "Katayama" disease. It seems that Asiatic schistosomiasis, or, as it is otherwise known, urticarial fever, is not uncommon in these countries and is associated with the presence of parasites in the vessels of the alimentary canal and elsewhere and with eosinophilia, urticaria, and fever. Cirrhosis of the liver together with its attendant ascites is usually a late manifestation, occurring from three to five years after infestation. Another form of parasitic liver disease is attended by the deposition of schistosome eggs in the liver, the ova acting as foreign bodies which give rise to focal granulomas associated with the formation of multinuclear giant cells of the Langhans type. Until the year 1926 Cutler [1] was able to collect reports of only 22 cases of schistosomiasis occurring in the United States and Canada. However, that the incidence of the disease is apparently increasing in North America is indicated by the fact that since 1933 five cases have been subjected to necropsy at Bellevue Hospital alone.

REPORT OF CASES

CASE 1.—E. L., aged 45, a native of the French West Indies, was admitted to Bellevue Hospital because of swelling of the legs and abdomen. The patient stated that he consumed 5 or 6 oz. (150 or 180 cc.) of rum daily. On admission, examination revealed physical signs of ascites, dilated superficial abdominal veins, and edema of the legs. Death occurred Dec. 31, 1933.

Necropsy.—The body was that of a poorly nourished adult white man weighing approximately 145 lb. (65.8 kg.). When the abdomen was opened, 500 cc. of serosanguineous fluid was removed. The liver was greatly diminished in size, and the surface was diffusely nodular, the individual nodules measuring from 2 to 5 mm. On section the organ cut with resistance and presented a granular appearance. The liver weighed 1,500 gm. Microscopically, the substance of the organ was divided into islands of variable sizes by overgrowth of connective tissue. In a branch of the portal vein near the porta hepatis there was an area of fibrosis in which schistosome ova were present. Another part of the same vein contained a solitary granuloma consisting of lymphocytes and eosinophils together with a giant cell which enclosed a well-preserved ovum. Near the walls of one of the larger intrahepatic branches of the portal vein were half a dozen schistosome ova lying in a matrix of lymphocytes, eosinophils, and an occasional polymorphonuclear neutrophil. The spleen was absent, having been removed at operation. On removal the organ measured 22.5 by 10 by 7 cm. Microscopic examination showed diffuse dilatation of the sinuses, hyperplastic lymph follicles, and irregularly scattered areas of fibrosis, hyalinization, and calcification in the walls of the central arteries. No ova were detected. The rest of the organs showed nothing of interest in the present connection.

CASE 2.—A 38-yr.-old Puerto Rican was admitted to Bellevue Hospital with the symptoms and signs of gastric ulcer and died Dec. 24, 1948, as a result of profuse hematemesis.

Necropsy.—The body was that of a poorly nourished man. On section the abdominal cavity was seen to be filled with blood clot. After the clot was removed, the lower edge of the liver was found to extend 8 cm. below the right costal margin. On removal the organ weighed 2,200 gm. It was greenish-yellow, firm, and diffusely nodular. The rest of the organs showed nothing of interest in the present connection. Microscopic examination of sections removed from seven different parts of the liver showed in all of them widespread overgrowth of the perilobular connective tissue. In one of the sections there was a solitary, small, circumscribed granuloma lying among the parenchyma cells. It consisted practically exclusively of eosinophils arranged around a hyalinized schistosome ovum.

CASE 3.—A 21-yr.-old Puerto Rican woman was admitted to Bellevue Hospital complaining of shortness of breath and swelling of the legs. On admission she presented the signs of an enlarged heart, with mitral insufficiency and mitral stenosis, together with swelling of the legs and abdomen and extreme dyspnea.[2] At necropsy the liver was small, weighing 960 gm. The consistency was increased, and the cut surface revealed numerous irregularly outlined dark-red areas. Microscopically, the structural unit consisted of a central vein surrounded by compressed liver cells, between which were collections of densely packed and partially autolyzed erythrocytes. In addition, there were patchlike areas of interlobular fibrosis. Many small granulomas were present in various parts of the liver and consisted of lymphocytes, eosinophils, and plasma cells arranged around the ova of schistosomes with or without the presence of multinuclear giant cells. Microscopically, schistosome granulomas were also found in the pancreas, the cortex of the kidney, the myocardium, and the lung.

CASE 4.—A 24-yr.-old Puerto Rican woman died in Bellevue Hospital on April 30, 1950. There was nothing in the clinical history worthy of note in the present connection, except, perhaps, that death apparently was due to extensive thoracic and abdominal lymph-node tuberculosis.

Necropsy.—The body was that of a fairly well-nourished woman, weighing about 130 lb. (59.0 kg.). When the abdomen was opened, the liver was found greatly enlarged, the lower edge lying 10 cm. below the costal margin in the right midclavicular line. On removal the organ weighed 2,250 gm. The capsule was smooth and glistening, the substance yellowish, and the lobular pattern was well preserved. The thoracic and paraaortic retroperitoneal lymph nodes were markedly enlarged and, on section, were almost completely caseous. The rest of the organs showed nothing of interest in the present connection. Microscopically, the lymph nodes showed epithelioid tubercles with extensive conglomerate areas of coagulation necrosis. In the liver parenchyma were a few small, rounded granulomas composed of eosinophils, lymphocytes, and an occasional polymorphonuclear neutrophil, among which were multinuclear giant cells arranged around schistosome ova in various stages of disintegration. Granulomas of similar or identical structure

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From the Laboratories of Pathology, Bellevue Hospital.

1. Cutler, M.: Bilharziasis in the United States and Canada, J. A. M. A. **86**: 816 (March 20) 1926.

2. Clark, E., and Graef, I.: Chronic Pulmonary Arteritis in Schistosomiasis Mansoni Associated with Right Ventricular Hypertrophy: Report of a Case, Am. J. Path. **11**: 693, 1935.

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were found in the mucosa and immediately adjacent submucosa of the colon, in the lungs, and in the interstitial tissues of the pancreas.

CASE 5.—A 30-yr.-old Puerto Rican man on admission to Bellevue Hospital revealed signs of pulmonary tuberculosis with cavitation. Otherwise, the clinical history contained nothing of interest in the present connection.

Necropsy.—The body was that of a well-developed, moderately well-nourished man. Examination of the various organs showed nothing of interest, with the possible exception of the liver, which weighed 1,500 gm. and, on both inspection and section, appeared to be normal. Microscopic examination of sections removed from three different parts of the liver showed in one of them a small, solitary, circumscribed granuloma lying among the parenchymal cells near the surface. The granuloma consisted of a preponderance of lymphocytes surrounding a hyalinized, twisted and distorted schistosome ovum. Except for scattered foci of fat vacuoles, the rest of the liver was well preserved.

SUMMARY AND CONCLUSIONS

In two of the five cases synopsized, cirrhosis of the liver was present and was attended by focal schistosomal granulomas lying in the walls of blood vessels or among the parenchymal cells, while cirrhotic changes occupied the perilobular spaces and arose independently of parasitic granulomas. In a third case the liver was the seat of chronic passive congestion, together with patchlike areas of interlobular fibrosis. Scattered throughout were numerous small granulomas consisting of variable numbers of eosinophils, lymphocytes, and plasma cells, with or without multinuclear giant cells arranged around the ova of schistosomes. In the remaining two cases the changes in the liver were limited practically exclusively to the presence of occasional parenchymal granulomas formed around schistosome ova. It is scarcely conceivable that relatively innocuous foreign bodies such as ova, acting alone, are capable of causing perilobular cirrhosis of the liver but that, when cirrhosis of the liver is associated with parasitic disease, such as schistosomiasis, the cirrhotic changes are to be attributed, most likely, to the miserable dietary conditions under which these patients live.

140 E. 28th St.

COMPLICATIONS AND SURGICAL TREATMENT OF HIATUS HERNIA AND SHORT ESOPHAGUS WITH THORACIC STOMACH

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and
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In 1933, Äkerlund [1] offered a simple classification of esophageal hiatus hernias. The three basic types are (1) short esophagus with thoracic stomach; (2) normal esophagus with paraesophageal hernia; (3) normal esophagus with pulsion type hernia.

Harrington's [2] excellent reports on the embryology, anatomy, and therapy of the various hiatal hernias have stimulated interest in their clinical recognition. The erroneous concept that hiatus hernia is a benign, structural curiosity incapable of serious portent is rapidly declining.

The least common of the hiatal hernias is that type associated with true short esophagus. Certainly it is less commonly recognized by the clinician and the roentgenologist than are the more obvious paraesophageal hernias. Endoscopists have called attention to short esophagus for years and, for the most part, have inherited the management of the disease. With the general lack of interest and failure in recognition, there has been associated unawareness of the serious possibilities of acquired short esophagus. Likewise, the development of satisfactory therapy has not kept pace with that of the commoner lesions observed elsewhere in the gastrointestinal tract.

COMPLICATIONS OF SHORT ESOPHAGUS

Careful distinction must be made between symptoms and complications in evaluation of the extent of the disease process and its response to conservative therapy. The majority of patients with acquired short esophagus have symptoms of dyspepsia, esophageal pain, dysphagia, nocturnal distress, and retrosternal discomfort. The development of peptic ulcer or severe anemia is indicative of major complication and is not a part of the true symptom complex.

The complications of acquired short esophagus and its associated thoracic stomach (Fig. 1) may be classified simply in three categories:

1. Bleeding—Massive or Occult
   a. Hematemesis
   b. Melena
2. Peptic Ulcer
   a. With bleeding
   b. With perforation
3. Stricture

Bleeding.—This appears to be the commonest complication of symptomatic short esophagus. In our experience the bleeding is usually occult. The patient may be entirely unaware of the significance of black stools, attributing this occurence to diet or medications. In five of our cases, the hemoglobin level has been below 7.0 gm., without the patient's comprehension of blood loss.

Periodic, severe hematemesis does occur. During 1950, we saw three patients who required emergency

From the Cleveland Clinic and the Frank E. Bunts Educational Institute.

Read at the Clinical Session of the American Medical Association, Cleveland, Dec. 5, 1950.

1. Äkerlund, A.: Die anatomische Grundlage des Röntgenbildes der Sogen: "Erworbenen Hiatusbrüche," Acta radiol. **14**: 523, 1933.

2. (*a*) Harrington, S. W.: Various Types of Diaphragmatic Hernia Treated Surgically, Surg., Gynec. & Obst. **86**: 735 (June) 1948. (*b*) Surgical Treatment of 105 Cases of Subdiaphragmatic Hernia, West. J. Surg. **44**: 255 (May) 1936. (*c*) Diagnosis and Treatment of Various Types of Diaphragmatic Hernia, Am. J. Surg. **50**: 381 (Nov.) 1940. (*d*) Surgical Treatment of More Common Types of Diaphragmatic Hernia, Ann. Surg. **122**: 546 (Oct.) 1945.

hospital admission because of hematemesis attributed to short esophagus. Each patient required multiple transfusions to reestablish and maintain blood volume. The frequency of hematemesis in patients with short esophagus has been commented on by Olsen,[3] Harrington,[2a] and Allison.[4] Certainly the incidence is sufficiently common to warrant consideration in any case in which there is unexplained vomiting of blood.

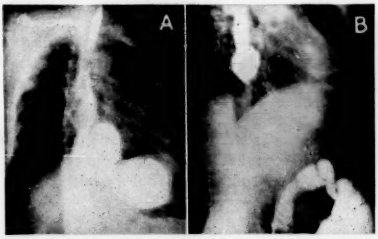

Fig. 1.—*A*, roentgenogram illustrating true short esophagus associated with large thoracic stomach in a woman, 60. The primary symptoms associated with this lesion were dyspepsia, melena, and severe secondary anemia. *B*, roentgenogram showing short esophagus in a man, 61, with history of intractable dyspepsia over an 18 year period.

Peptic Ulcer.—The association of ulceration with acquired short esophagus has been recognized for many years. In 1943, Allison [4] presented 10 cases of short esophagus with peptic ulceration. The diagnoses were based on clinical, roentgenologic, and esophagoscopic findings. Land [5] and Allison commented on the severity of the symptoms and the resistance to conservative therapy. American writers [6] as well have emphasized the association of peptic ulceration in short esophagus.

There seems to be little question that peptic ulcer may occur as either the initiating factor or as a secondary complication of short esophagus. When ulcer is present, there is an associated esophagitis and gastritis, which greatly impedes accurate localization. In the few patients on whom we have operated for intractable pain, bleeding, and dysphagia, the ulcer always has been in the thoracic stomach (Fig. 2); we have not seen true peptic ulcer within the esophagus at operation. In three cases the ulcer had perforated into the mediastinum; the sealed perforation involved the pericardium in one instance and the right lower lobe of the lung in another.

Stricture.—Dysphagia is the commonest symptom of short esophagus. Whereas dysphagia may be transient in nature and due to neurogenic cardiospasm, an organic stricture is the result of a severe inflammatory process such as long-standing esophagitis. The stricture is due to a cicatrizing contracture at the cardiac end of the esophagus. Occasionally a fibrous stricture may be found in short esophagus associated with scleroderma; apparently esophagitis is not a factor in this instance.

With development of stricture, there may be associated progressive shortening. The degree of "esophageal insufficiency" is not fixed necessarily. When the disease is acquired, the shortening is believed to be a reflex phenomenon with associated inflammatory and neurogenic factors. If the entity is unrecognized or its treatment inadequate, the shortening may be progressive. In severe cases, the esophagus may contract to approximately one-half of its expected normal length. The opportunity for a clinical cure may be lost if the disease progresses to the ultimate degree.

THERAPY

The management of short esophagus has been handled primarily by the endoscopist and gastroenterologist. Detailed programs of therapy have been offered by Olsen,[3] Polley,[7] Dick and Hurst,[8] Allison and associates,[4] and others. Elaboration of the measures described is not relevant at this time; in general, two methods of conservative therapy have been suggested: (1) dietary control with supplemental medication and (2) use of bougies for the relief of stricture.

In their excellent review of the pathology and therapy of short esophagus with complication, Allison and his co-workers,[4] state they are not convinced that any form of treatment offers cure. We are in accord with this statement. Careful medical therapy and periodic use of bougies often will alleviate the symptoms of short esophagus but cannot cure the structural abnormality. It seems logical, however, that the ideal therapy would involve restoration of the esophagus to normal length and reduction of the stomach to the abdominal cavity. Unless this is accomplished, any therapy, regardless of its intensity, must be considered as palliative only.

In evaluating the site of surgery for short esophagus, one must distinguish between the uncomplicated and complicated types. This statement may be amplified by a brief description of the methods of surgical treatment employed at the Cleveland Clinic.

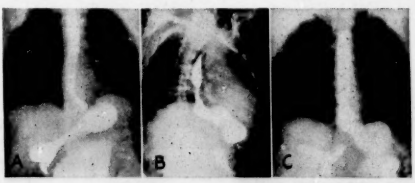

Fig. 2.—Examples of severely complicated short esophagus associated with peptic ulcer. *A*, perforating ulcer of thoracic stomach with direct extension into parietal pericardium. *B*, severe stricture with peptic ulcer of thoracic stomach perforating into lower lobe of right lung. *C*, short esophagus with penetrating peptic ulcer in thoracic stomach associated with intractable pain.

SURGICAL TREATMENT

Complicated Short Esophagus.—When short esophagus is associated with peptic ulcer, stricture, and severe anemia, evaluation of the primary disease is difficult. Prolonged hospitalization and intensive medical therapy have yielded poor results too frequently. Also it may be

3. Olsen, A. M., and Harrington, S. W.: Esophageal Hiatal Hernias of Short Esophagus Type, J. Thoracic Surg. **17**: 189 (April) 1948.

4. Allison, P. R.; Johnstone, A. S., and Royce, G. B.: Short Esophagus with Simple Peptic Ulceration, J. Thoracic Surg. **12**: 432 (June) 1943.

5. Land, F. T.: Congenital Short Esophagus with Thoracic Stomach, J. Laryng. & Otol. **61**: 641 (Dec.) 1946.

6. Harrington,[2a,b] Olsen and Harrington,[3] Putney, F. J.: Thoracic Stomach Produced by Esophageal Hiatus Hernia and Congenital Short Esophagus, Ann. Int. Med. **28**: 1094 (June) 1948.

7. Polley, H. F.: Congenital Short Esophagus with Thoracic Stomach and Esophageal Hiatus Hernias: Report of 47 Cases, J. A. M. A. **116**: 821 (March 1) 1941.

8. Dick, R. C. S., and Hurst, A.: Chronic Peptic Ulcer of Oesophagus and Its Association with Congenitally Short Oesophagus and Diaphragmatic Hernia, Quart. J. Med. **11**: 105 (April) 1942.

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impossible to exclude carcinoma by roentgen studies of esophagoscopy. The generally unsatisfactory responses in our experience, plus the uncertainty of diagnosis, have prompted a radical approach in selected cases.

We believe that surgical treatment of the patient with the complicated short esophagus is a serious undertaking. Satisfactory preparation for operation is not easy nor always possible. Anemia, malnutrition, and chronic disease increase the risk of surgery. Narcotic dependency is occasionally a factor in the patient with intractable pain due to penetrating ulcer.

The operation employed in these patients has been similar to that used for esophageal malignancy. Essentially it involves a transthoracic resection of the diseased esophagus and cardia with esophagogastrostomy (Fig 3). The long-standing inflammatory process produces severe reaction in the mediastinum, rendering the dissection considerably more tedious than is usual for esophageal tumor. Even at the time of surgery, it may be impossible to exclude the possibility of neoplasm.

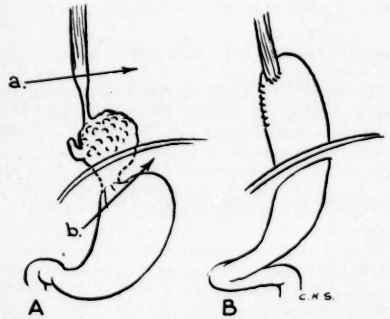

Fig. 3.—Schematic outline of surgical technic employed in complicated short esophagus associated with peptic ulcer as illustrated in Figure 2. *A*, arrows represent lines of resection with removal of diseased segment of esophagus and cardiac portion of stomach. *B*, diagram of completed esophagogastrostomy. Cardiac stomach has been resected and anastomosis effected on greater curvature and anterior wall of stomach.

We have performed this operation on six patients, all of whom were benefited. Actually the procedure is palliative in nature, since the patient with esophagogastrostomy is rarely a completely happy person. The operation does relieve the ulcer pain, stricture, and bleeding. We insist, however, on a prolonged medical regimen in which to manage the expected symptoms of thoracic stomach.

UNCOMPLICATED SHORT ESOPHAGUS

The term "uncomplicated" is used here to denote the absence of secondary physical changes altering the morphology of a short esophagus. In an effort to develop a simple definitive surgical procedure for correction of this defect, a distinction must be made between the structurally uncomplicated short esophagus and the complicated type described in the foregoing paragraphs. Actually the patient who presents the simpler lesion may have suffered any of the listed complications. With recognition of the limitations of conservative therapy for a structural defect, a search has been made for a simple corrective procedure. Harrington and Olsen have stated repeatedly that the logical treatment of symptomatic short esophagus would involve the reduction of the thoracic stomach within the abdomen. When this is possible, there may be permanent remission of symptoms. Adjunct procedures, including phrenic crush, gastrostomy, and vagotomy, have been attempted with indifferent results.

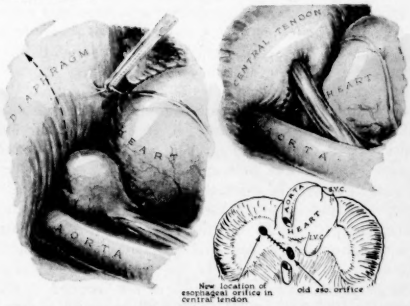

Fig. 4.—Artist's conception of anatomic features as viewed through thoracotomy incision during operation for structurally uncomplicated short esophagus with thoracic stomach.

Although the esophagus has been shortened experimentally by vagal stimulation,[9] we are unaware of any method by which the diseased organ is lengthened. In cases of minimal shortening, the defect between cardiac esophagus and hiatus may be bridged by traction and fixation after adequate mobilization of the esophagus. Sectioning of the vagus alone will permit lengthening by

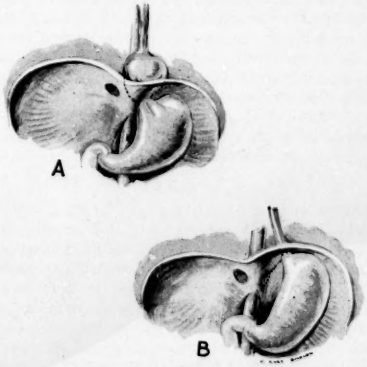

Fig. 5.—*A*, schematic representation of short esophagus with thoracic stomach and relation to leaves of diaphragm. *B*, reduction of stomach below diaphragm following paralysis of phrenic nerve and transplantation of esophageal hiatus to central dome of diaphragm.

traction, but the side effects of vagotomy may offset the advantage of such a procedure.

A comparatively simple operation has been used at the Cleveland Clinic, with promising results, in a small

9. Dey, F. L.; Gilbert, N. C.; Trump, R., and Roskelly, R. C.: Reflex Shortening of Esophagus in Experimental Animal with Production of Esophageal Hiatus Hernia, J. Lab. & Clin. Med. 31:499 (May) 1936.

series of cases. The operation is basically a transthoracic reduction of the stomach, with alteration in the diaphragmatic hiatus and phrenic paralysis (Figs. 4 and 5). Although the esophagus itself is not appreciably lengthened, the vertical diameter of the thoracic cavity is shortened.

The technic parallels the procedure described by Merendino, Varco, and Wangensteen [10] in correction of paraesophageal hiatus hernia. A thoracotomy is performed at the level of the eighth left rib, and the pulmonary ligament divided. The terminal esophagus and thoracic stomach are completely mobilized from within the mediastinum. The phrenic nerve is crushed, and the diaphragm is allowed to elevate. A site is selected for the new hiatus, and the diaphragm is incised from this point through the anatomic hiatus. Care must then be taken to free the stomach from its posterior and medial attachments along the crura of the diaphragm. Emphasis is placed on the necessity for complete mobilization of the terminal esophagus and thoracic stomach, with separation of the mediastinal and subdiaphragmatic attachments. It is not necessary for one to divide the gastrohepatic or gastrolienal ligaments. After mobilization is accomplished, the cardia of the stomach is brought laterally to the site of new hiatus; the right and left crura are approximated with interrupted double silk sutures, with resultant obliteration of the original hiatus medially and posteriorly to the cardia. The stomach is reduced below the diaphragm, and the tendinous portion is closed around the cardiac esophagus. One should observe care in tacking the new hiatus completely around the esophagus by means of interrupted silk sutures to prevent sliding or herniation. When the repair is accomplished, the cardiac stomach is at the highest point under the dome of the diaphragm, the position normally occupied by the fundus. Because the diaphragm is paralyzed, the dome is considerably elevated. The combination of new hiatus, plus phrenic paralysis, greatly diminishes the distance traversed by the esophagus. In this way, a previously short esophagus may be adequate in length. Although the esophagus itself is not lengthened, the required span is shortened.

COMMENT

Greater emphasis must be placed on the recognition of short esophagus and its associated complications. Special technics used by the experienced roentgenologist, including examinations in the Trendelenburg position, are of paramount importance. Inadequacy of medical therapy for short esophagus is largely due to the frequent erroneous diagnosis of duodenal ulcer. With early recognition of the entity and adequate medical therapy, the patient may be spared prolonged discomfort and serious complication.

When serious complications have ensued and the disease is refractory to therapy, the possibilities of surgical relief must be considered. Whereas the outright indications for surgery are by no means crystallized in our minds, we believe that a more radical approach will be employed in the future. It must always be borne in mind that short esophagus is a structural defect that cannot be reduced by conservative measures. Although the symptoms may be relieved in many cases by intensive medical therapy, the program must be continued through life, since the underlying cause of the symptoms remains. We feel that there is an excellent possibility that surgery will offer permanent relief in selected cases.

Cleveland Clinic (Dr. Effler).

10. Merendino, K. A.; Varco, R. L., and Wangensteen, O. H.: Displacement of Esophagus into New Diaphragmatic Orifice in Repair of Para-Esophageal and Esophageal Hiatus Hernia, Ann. Surg. **129**: 185 (Feb.) 1949.

CLINICAL NOTES

APLASTIC ANEMIA COMPLICATING STREPTOMYCIN TREATMENT OF PULMONARY TUBERCULOSIS

REPORT OF A CASE, WITH RECOVERY

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and
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The major toxic manifestations accompanying prolonged streptomycin therapy are well known. Renal damage, vestibular dysfunction, dermatitis, and other sensitivity reactions have all been observed. The reported incidence of blood dyscrasias, however, has been very low. The initial report of the Streptomycin Committee of the Veterans Administration and offices of the Surgeons General of the Army and Navy,[1] stated that of 800 patients treated with streptomycin, in five (0.7%) relatively mild leukopenia with neutropenia developed. One case of agranulocytosis occurred in a patient with miliary tuberculosis. These reactions were felt to be quite definitely caused by streptomycin in the sense that they were alleviated by its withdrawal. Deyke and Wallace [2] recently reported two cases of aplastic anemia, one of which terminated fatally, during streptomycin therapy of 400 patients with tuberculosis at Fitzsimons General Hospital. Autopsy of the fatal case revealed pronounced hypoplasia of the bone marrow. In reviewing the toxic manifestations encountered during the treatment of 57 patients in the Cornell-New York Hospital series, McDermott [3] reported that relative granulocytopenia had been observed in a few cases with acute hematogenous tuberculosis. The total leukocyte counts eventually rose to within normal range despite the continuation of streptomycin therapy. In one patient with acute brucellosis, who had been receiving 6 gm. of streptomycin daily, thrombocytopenia developed. Recovery was prompt and complete after the discontinuation of

Dr Lawrence M. Serra kindly permitted us to study this patient.
Baltimore Rh Laboratory Fellows in Medicine (Drs. Bradford and Spurling).

From the Department of Medicine, University of Maryland School of Medicine.

1. The Effect of Streptomycin upon Pulmonary Tuberculosis: Preliminary Report of a Cooperative Study of 223 Patients by the Army, Navy and Veterans Administration, Am. Rev. Tuberc. **56**: 485-605 (Dec.) 1947.
2. Deyke, V. F., and Wallace, J. B.: Development of Aplastic Anemia During the Use of Streptomycin: Report of 2 Cases, J. A. M. A. **136**: 1098 (April 24) 1948.
3. McDermott, W.: Toxicity of Streptomycin, Am. J. Med. **2**: 491-500 (May) 1947.

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streptomycin. A recent report [4] of the Veterans Administration Streptomycin Committee stated that in 5.2% of 1,751 patients treated with streptomycin some type of blood dyscrasia developed.

We wish to report a case of aplastic anemia, which occurred as a complication of streptomycin therapy of pulmonary tuberculosis. The patient eventually recovered.

REPORT OF A CASE

H. W., a white housewife, aged 35, was first admitted to the University Hospital on Aug. 27, 1945. She had been in good health until four months prior to admission, when she noted the onset of dyspnea, nervousness, anorexia, and weight loss. Two months prior to admission she had been seen by a physician who suspected the existence of hyperthyroidism and advised hospitalization.

The family history revealed that her father had died of tuberculosis. Review of her past history disclosed an episode of pneumonia at 1 yr. of age. At the age of 9 yr. she had an acute bout of fever and painful swollen knee joints. No diagnosis was made at that time, but she was later told she had rheumatic heart disease with valvular damage. The patient had two attacks of acute pyelitis in 1929 and in 1931. There were two uneventful pregnancies. A review of systems revealed frequent acute respiratory infections.

On physical examination the patient appeared poorly nourished and chronically ill. There was a slight generalized enlargement of the thyroid gland. A harsh blowing systolic murmur was heard in the mitral area. The heart was not enlarged. Examination of the chest revealed limitation of motion on the right side. There was marked dullness to percussion at the right apex posteriorly from the first to the fourth ribs. Breath sounds were decreased and tactile fremitus was increased over this area. No rales were heard. The left lung was normal. The remainder of the physical examination was essentially normal.

Admission laboratory studies revealed the following data: red blood cell count, 4,250,000 per cubic millimeter; hemoglobin value, 13 gm.; leukocytes, 10,200 per cubic millimeter, with a differential count of 60% neutrophils, 28% lymphocytes, and 12% monocytes; platelets, 310,000 per cubic millimeter. Routine urine and stool examinations were noncontributory. All blood chemical studies were within normal limits. An electrocardiogram did not indicate any deviations from normal. Repeated basal metabolism rates were normal. An x-ray of the chest revealed a large amount of patchy infiltration involving the right lung from the apex to the anterior end of the sixth rib. Similar infiltration was present in the left lung, from the first to the fourth interspaces. No definite cavities were noted. The cardiac shadow was normal. On Aug. 31 sputum examination was positive for tubercle bacilli.

The patient did not receive any therapy while hospitalized. She was discharged on Sept. 6, 1945, arrangements having been made for her to be treated at home by a chest specialist. A right pneumothorax was performed and maintained. The patient was kept on strict bed rest for 12 mo. Sputum examinations became negative and moderate activity was allowed. The patient gained weight and improved over a two-year period. Serial x-rays of the chest revealed no change in the left lung. The pneumothorax was constantly maintained on the right.

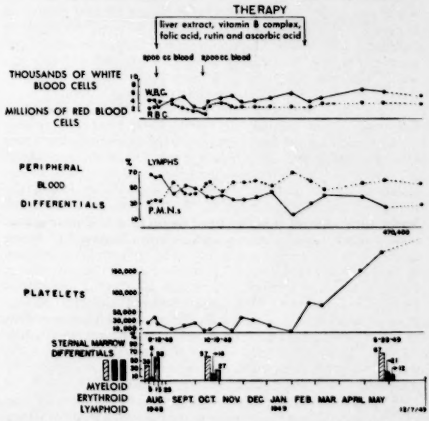
On Feb. 20, 1948, her sputum again became positive for acid-fast organisms. Because of this finding, the patient was placed on strict bed rest and started on intramuscular streptomycin, 0.8 gm. daily (16 mg. per kilogram). She continued to receive this dose until June 20, 1948, a period of 122 days. The total dose of streptomycin given was 98 gm. During this period the lesion in her left lung cleared considerably and she felt much improved. Sputum examinations became negative and other routine laboratory studies were said to have been within normal limits.

In July 1948, she contracted an acute respiratory infection after which she noted the appearance of marked pallor, recurrent elevations of temperature, and numerous petechiae and purpuric spots on the extremities. Several episodes of spontaneous epistaxis occurred. She was seen by her physician, and hospitalization was again advised.

The patient was readmitted to the hospital on Aug. 5, 1948. The significant physical findings consisted of marked pallor of the skin and mucous membranes, numerous petechiae over the extremities and trunk, several large ecchymotic areas on the extremities, a right pneumothorax, and a systolic and rumbling presystolic murmur over the mitral area. Remainder of the physical examination was essentially noncontributory.

Admission laboratory studies revealed a red blood cell count of 2,980,000, a hemoglobin value of 10.2 gm., 4,850 leukocytes with a differential count of 34% neutrophils and 66% lymphocytes, and platelets, 23,840 (counted by Olef's method). All blood chemical studies were within normal limits. The bleeding time was 2 min. 45 sec.; the coagulation time (Lee-White), 7½ min.; clot retraction was not complete in 24 hr. The prothrombin time was 18 sec. with a control of 18 sec. The capillary fragility test was markedly positive. Several blood cultures and sputum examinations were negative. X-ray of the chest revealed a right pneumothorax with an excellent degree of collapse. There was slight patchy infiltration demonstrable in the upper left lung. No specific cavitation was present.

She was given 2,000 cc. of whole blood, and, although the red blood cell count and hemoglobin value returned to normal levels, the leukopenia and thrombocytopenia persisted (chart). The



Summary of patient's course and treatment.

differential count continued to show a high percentage of mature lymphocytes. Sternal bone marrow examination was done on Aug. 18, 1948. The smears showed a marked decrease in cellularity, the predominant cells being small mature lymphocytes. Differential count was as follows: myeloblasts 3%, promyelocytes 2%, myelocytes 2%, metamyelocytes 12%, segmented neutrophils 17%, mature lymphocytes 58%, and erythroid elements 6%. Megakaryocytes were not observed. A diagnosis of hypoplastic anemia with secondary thrombocytopenia was made.

A therapeutic regimen consisting of liver extract, intramuscular vitamin B complex, folic acid, rutin, and ascorbic acid was initiated. The patient was discharged from the hospital on Aug. 24, 1948, by which time the fever had subsided and the hemorrhage tendency had become less marked. The blood studies on that day were as follows: red blood cell count, 4,050,000; hemoglobin value, 11.6 gm.; 3,000 leukocytes with a differential count of 70% lymphocytes, 27% neutrophils, 2% eosinophils and 1% monocytes; platelets, 35,000.

Periodic blood studies were made during the next six weeks and therapy was continued as before. Occasional spontaneous epistaxis and small showers of petechiae occurred. Menstrual periods were somewhat prolonged and profuse. Slight hematuria

4. Streptomycin in the Treatment of Tuberculosis, report of the Council on Pharmacy and Chemistry, J. A. M. A. 138: 584-593 (Oct. 23) 1948.

was also observed on several occasions in September. On Oct. 1, 1948, marked pallor of the skin and mucous membranes was again noted. Laboratory studies revealed a red blood cell count of 2,390,000, hemoglobin value of 7.4 gm., 3,050 leukocytes, with a differential count of 44% neutrophils, 48% lymphocytes, 6% monocytes, and 2% eosinophils, and 27,600 platelets.

She was readmitted to the hospital on Oct. 16, 1948. Marked pallor, numerous petechiae, and several ecchymotic areas were noted on the extremities. The red blood cell count was 1,910,000 and the hemoglobin value was 6.6 gm. The patient was again given 2,000 cc. of whole blood over a period of four days. Bone marrow examination on Oct. 18 revealed a moderate increase in cellularity as compared to the marrow previously examined. The differential count was as follows: myeloblasts 3.5%, promyelocytes 4.0%, myelocytes 9.5%, metamyelocytes 17.0%, segmented neutrophils 23.5%, mature lymphocytes 25%, monocytes 1%, plasma cells 1%, and erythroid elements 15.5%.

The patient was discharged from the hospital on Oct. 19, 1948, somewhat improved. She continued on the therapeutic regimen noted above. For a period of several months thereafter there was gradual clinical and hematological improvement. The hemorrhagic manifestations diminished. The red blood cell count was maintained between 3½ and 4 million without further transfusions. The white blood cell count fluctuated between 4,000 and 6,000, and the differential counts became normal in December, 1948. However, the thrombocytopenia persisted. In February, 1949, blood studies were as follows: red blood cell count 3,500,000; hemoglobin value 11.4 gm.; 6,600 leukocytes with a differential count of 74% neutrophils, 18% lymphocytes, 6% monocytes, and 2% eosinophils; platelets 3,300.

The vitamin B complex and folic acid were discontinued in February. From February to April, 1949, there was further hematologic improvement. The platelet level rose steadily. Liver extract was discontinued in March, 1949. Blood studies on April 27, 1949, revealed a red blood cell count of 4,480,000; hemoglobin value of 13.8 gm.; 7,300 leukocytes with a differential count of 59% neutrophils, 39% lymphocytes, and 2% monocytes, and 140,800 platelets. On May 25, 1949, another bone marrow aspiration was performed. Examination of the smears revealed normal cellularity. The differential count was as follows: myeloblasts 1.0%, premyelocytes 5.0%, myelocytes 10%, neutrophilic metamyelocytes 31%, segmented neutrophils 19.5%, lymphocytes 13.0%, and erythroid elements 20.5%. Several megakaryocytes were seen. Peripheral blood studies were as follows: red blood cell count, 4,520,000; hemoglobin value, 3.3 gm., 5,700 leukocytes with a differential count of 61% segmented neutrophils, 32% lymphocytes, 4% monocytes, 2% eosinophils, and 1% basophils; platelets, 200,000.

In Aug. 1949, progression of the tuberculous process in the left apex necessitated readmission to the hospital for performance of a lucite plumbage. The patient withstood the procedure well and had no unusual hemorrhagic phenomena. The blood picture was essentially normal at this time except for moderate thrombocytopenia (260,000 per cubic millimeter). When last seen on Dec. 7, 1949, she was completely asymptomatic, had gained weight, and presented the following blood picture: red blood cell count, 4,970,000; hemoglobin value, 14.1 gm.; 6,600 leukocytes with a differential count of 58% neutrophils, 33% lymphocytes, 6% monocytes, 2% eosinophils, and 1% myelocytes; platelets, 470,400.

COMMENT

When first seen in 1945, prior to streptomycin therapy, the patient's peripheral blood picture was essentially normal. During the four-month period of streptomycin administration she was at home, and there were no recorded blood counts. Several weeks after discontinuance of the drug, purpuric manifestations appeared. On admission to the hospital, detailed study revealed a picture compatible with the diagnosis of aplastic anemia. There was no history of exposure to other agents or drugs which have been reported to produce hypoplasia of the bone marrow, nor was there any evidence of miliary spread of the tuberculous infection.

During the first six months after streptomycin had been discontinued, very little hematological improvement occurred in spite of supportive therapy. The leukocyte count and differential pattern became essentially normal by December, 1948, approximately six months after onset of illness. The hemoglobin and red blood cell values rose to normal during the next three months. The platelets, on the other hand, did not reach normal until approximately 16 mo. after onset. It is interesting to note that during the last hospital admission (August, 1949) when exacerbation of the tuberculous process had occurred, no hematological regression was observed. The most recent blood studies indicate an essentially normal picture.

The evidence incriminating streptomycin as the agent responsible for the aplastic anemia in this case is, of course, only circumstantial. One must consider first the influence of tuberculosis itself on the hematopoietic system. It is well known that anemia, granulocytopenia, and/or thrombocytopenia have been observed in acute hematogenous tuberculosis with bone marrow involvement. A decrease in granulocytes and/or platelets has also been observed following the injection of tuberculin in patients with active pulmonary tuberculosis.[5] The latter observation led to the suggestion that perhaps a similar mechanism may be responsible for the granulocytopenia and thrombocytopenia occasionally seen in such patients. However, a careful search of the literature failed to reveal typical cases of aplastic anemia due to tuberculosis per se except when miliary spread was present. The case presented here displayed no evidence of miliary dissemination.

The mechanism of the development of hypoplasia of the bone marrow during streptomycin therapy is unknown. No evidence exists for a direct toxic effect on the hematopoietic system. However, bone marrow hypoplasia can occur as a result of the creation of a folic acid deficiency.[6] Lucherini and Schiavetti[7] observed that streptomycin administered orally to rats and chickens produced a macrocytic anemia, granulocytopenia, and hypoplasia of the bone marrow. The peripheral blood picture as well as the bone marrow was rapidly restored to normal by the oral or parenteral administration of folic acid. The experiments seemed to indicate that, at least in rats and chickens, the bacterial flora of the intestinal tract plays an important part in the synthesis of folic acid. It was suggested that the toxic hematopoietic effect of streptomycin was due to its bactericidal action on the intestinal flora. The possibility that prolonged administration of streptomycin may, as a result of its effect on the bacterial flora of the human intestinal tract, produce a folic acid deficiency must be considered. This could result in hypoplasia of the bone marrow.

In the treatment of acute leukemia with the folic acid antagonists, some authors [6b] have observed hypoplasia of

5. Muller, G. L.: Clinical Significance of the Blood in Tuberculosis, New York, Commonwealth Fund, 1943, chap. 2.

6. (*a*) Jukes, T. H., and Stokstad, E. L. R.: Pteroylglutamic Acid and Related Compounds, Physiol. Rev. **28**: 51-106 (Jan.) 1948. (*b*) Sacks, M. S.; Bradford, G. T., and Schoenbach, E. B.: The Response of Acute Leukemia to the Administration of Folic Acid Antagonists Aminopterin and Amethopterin: Report of 14 Cases, Ann. Int. Med. **32**: 80-115 (Jan.) 1950.

7. Lucherini, T., and Schiavetti, L.: Experimental Macrocytic Anemia from Oral Administration of Streptomycin, and Restoration of Blood Picture to Normal by Administration of Folic Acid, Policlinico (Sez. prat.) **55**: 65-73 (Jan. 19) 1948.

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the bone marrow, ulcerative stomatitis, alopecia, and diarrhea. Beham and Perr [8] have reported the development of an ulcerative aphthous stomatitis in three patients with pulmonary and extrapulmonary tuberculosis during streptomycin therapy. The hematological picture was not discussed, but the description and photographs of the ulcerative stomatitis appeared quite similar to that observed by us in patients with a folic acid deficiency induced by the therapeutic use of folic acid antagonists.

Since streptomycin therapy has become widespread in the treatment of many human infections, the minor toxic manifestations will probably assume greater importance. At the present time, it would seem advisable to consider anemia, granulocytopenia, and thrombocytopenia collectively as a manifestation of streptomycin toxicity and an indication for the immediate discontinuation of therapy.

SUMMARY

A case of aplastic anemia following prolonged administration of streptomycin is presented. Gradual recovery took place over a period of 16 mo. after the discontinuation of the drug.

It is suggested that prolonged courses of streptomycin, by virtue of an effect upon the bacterial flora of the human intestinal tract, may produce a folic acid deficiency with subsequent hypoplasia of the bone marrow.

8. Beham, H., and Perr, H.: Stomatitis Due to Streptomycin, J. A. M. A. **138**: 495-496 (Oct. 16) 1948.

THROMBOPENIC PURPURA DURING STREPTOMYCIN TREATMENT OF TUBERCULOUS EMPYEMA

REPORT OF A CASE

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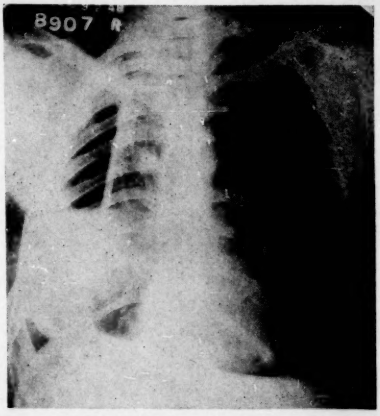
and
Seymour Fisher, M.D., Phoenix, Ariz.

Incidence of severe toxic reactions in the hematopoietic systems of patients treated with streptomycin has been very small. The Central Streptomycin Committee of the Veterans Administration reported only 0.6%-2.3% of blood dyscrasias in 1,751 patients treated under streptomycin regimens in the federal hospitals.[1] The great majority of these reactions consisted of relatively mild leukopenia and granulocytopenia; however, two cases of aplastic anemia apparently caused by streptomycin were reported by Deyke and Wallace.[2] A. M. Walker,[3] secretary of the Central Streptomycin Committee, informed us that he knew of no case of thrombopenic purpura occurring during the administration of streptomycin in any patient treated in the United States. In one patient with miliary tuberculosis treated with streptomycin by Feld [4] agranulocytosis developed. Benhamou and others [5] reported that in one child with tuberculous meningitis, treated with 2 gm. of streptomycin daily, agranulocytosis with purpura developed on the 30th day of therapy, and the child died within 48 hr. Keefer and others,[6] in a report of 1,000 cases treated with streptomycin, mentioned one case of purpura hemorrhagica occurring in a patient treated with streptomycin. Since no details were given, the case presumably was fairly mild. To our knowledge there has been no instance in the American literature of severe thrombopenic purpura developing during or after streptomycin therapy. It may, therefore, be of interest to report one such case occurring in a patient treated with streptomycin, bringing to the attention of the medical profession the possibility of such a reaction, especially when a patient has a history of previous administration of this antibiotic.

REPORT OF A CASE

History.—B. S., a white man aged 32, gave a history suggestive of pulmonary tuberculosis since July, 1946, that was confirmed bacteriologically and by x-ray studies a month later when a diagnosis of active pulmonary tuberculosis of the right upper lobe was made. Pneumothorax was started on the right side in September, 1946, and was followed by pneumonolysis. The patient responded well to therapy; smears and cultures of his sputum and gastric contents became negative for acid-fast bacilli.

During April, 1947, a course of streptomycin was started, but after the administration of only 2 gm. over a period of two days, further antibiotic therapy was refused by the patient because of local burning pain. About May, 1948, a tuberculous empyema developed on the right side; the patient was treated by repeated aspirations and irrigations of the pleural cavity with chloroazodin (azochloramid®) solution. There was some improvement in his condition.



Roentgenogram of chest, Sept. 2, 1948, showing tuberculous empyema.

Physical Examination and Laboratory Data.—On Aug. 31, 1948, he was admitted to Billings Veterans Administration Hos-

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

1. Streptomycin in Treatment of Tuberculosis, Report of the Council on Pharmacy and Chemistry, J. A. M. A. **138**: 584 (Oct. 23) 1948.

2. Deyke, V. F., and Wallace, J. B.: Development of Aplastic Anemia During the Use of Streptomycin: Report of 2 Cases, J. A. M. A. **136**: 1098 (April 24) 1948.

3. Walker, A. M.: Personal communication to the authors.

4. Feld, D. D.: Agranulocytosis During the Streptomycin Treatment of Miliary Tuberculosis, Am. Rev. Tuberc. **59**: 317, 1949.

5. Benhamou, E.; Destaing, F., and Cholal, A.: Blood Accidents in Course of Treatment with Streptomycin, Presse méd. **56**: 517, 1948.

6. Keefer, C. S., and others: Streptomycin in Treatment of Infections: A Report of 1,000 Cases, J. A. M. A. **132**: 70, 1946.

pital, where a physical examination seemed to indicate that he was in good general condition. His temperature was 98.4 F.; pulse, 80; blood pressure, fluctuating between 156/92 and 126/90. No history suggestive of any previous blood dyscrasias was elicited; no signs of petechiae or ecchymoses were noted. His medication consisted of vitamins, and occasional phenobarbital and secobarbital (seconal®) sodium.

Operation.—Because of a markedly thickened pleura interfering with reexpansion of the right lung, tuberculous empyema, and extensive nodular involvement of the right upper lobe, a decortication of the right lung and a five-rib thoracoplasty were performed by Dr. L. Nehil on Oct. 29, 1948, and Nov. 15, 1948, respectively.

On Oct. 28, 1948, in anticipation of surgery, streptomycin therapy had been started, 0.5 gm. being given twice a day for 25 days. Penicillin (50,000 units every three hours) was administered at the same time for 26 days. On Oct. 30, 1948, the phenomenon was markedly positive. Clot retraction, on Nov. 28, 1948, was reported to be very poor in five hours; a few days later, only slight clot retraction was noted in 24 hr. There was a very marked decrease in blood platelets, none being observed in 1,000 cells on Dec. 3, 1948. Examination of urine repeatedly showed gross blood and 4+ albumen, and (on microscopic examination) innumerable red blood cells and white blood cells were seen. The prothrombin percentage fluctuated between 85% and 95%; icterus index, between 5 and 8. The red blood cell fragility and congo-red test were essentially normal. Numerous sputum examinations and gastric contents examinations, including four cultures, were negative for acid-fast bacteria. The patient was tested with a 1:8,000 streptomycin solution intracutaneously; an ecchymosis was found the next day at the test site. This test was hard to interpret because of a tendency for ecchymoses to develop in the patient after a mild trauma. On Dec. 28, 1948, Dr. P. J. Fouts reported that a bone marrow smear showed some

Laboratory Findings in a Case of Thrombopenic Purpura

Date	Erythrocytes (Millions per Cu. Mm.)	Leukocytes (Thousands per Cu. Mm.)	Hemoglobin (Gm.)	Neutrophils (%)	Lymphocytes (%)	Monocytes (%)	Eosinophils (%)	Platelets (Thousands per Cu. Mm.)	Bleeding Time (Min., Sec.)	Coagulation Time (Min., Sec.)	Clot Retraction Time	Urine Examination
8/ 4/48	5.26	13.6	15.7	66	26	2	6	....	.....	.....	.....	Negative
9/ 1/48	....	11.1	....	65	31	3	..	....	.....	.....	.....	Negative
10/26/48	4.97	9.5	15.0	58	42	..	..	....	1; 55	4; 48	.....	Negative Rare WBC
11/ 3/48	3.18	6.9	9.5	76	24	..	..	....	.....	.....	.....	1-3 WBC Negative
11/ 8/48	3.86	....	12.0	..	..	..	..	....	.....	.....	.....	.....
11/15/48	2.79	11.7	8.5	75	16	4	5	....	.....	.....	.....	.....
11/18/48	2.73	....	8.5	..	..	..	..	....	.....	.....	.....	Negative
11/22/48	3.43	9.4	10.5	62	28	5	5	....	.....	.....	.....	.....
11/24/48	3.49	9.3	11.0	85	14	1	..	....	3; 30	7; 00	.....	Gross blood and many RBC
11/28/48	3.21	....	10.0	80	20	..	..	....	.....	.....	Very poor at 5 hr.; none at 2 hr.	.....
11/30/48	....	....	....	..	..	..	..	None seen	5; 00	5; 00	Slight retraction	.....
12/ 3/48	4.1	9.5	13.5	66	27	4	2	in 1,000 cells			in 24 hr.	
12/10/48	....	....	....	..	..	..	..	....	.....	.....	Slight retraction after 24 hr.	Many RBC Albumin (trace)
12/14/48	....	....	....	..	..	..	..					
12/15/48	5.21	10.8	16.0	66	32	2	..	....	.....	.....	.....	Many RBC Albumin 4+
								32.0	7; 37	.....	.....	
12/27/48	5.41	9.5	15.0	80	18	2	..	40.0	3; 42	4; 10	Very poor after 8 hr.	1-3 RBC per high power field
12/30/48	4.3	12.1	....	65	28	3	4	....	3; 25	5; 55	Very poor after 8 hr.	Negative
1/ 9/49	4.43	10.85	15.0	..	..	..	..	....	4; 40	5; 55	Very poor after 6 hr.	Negative
1/16/49	4.36	....	....	..	..	..	..	58.0	14; 00	7; 00	Very poor	.....
1/26/49	4.02	14.4	13.5	72	20	2	5	....	.....	.....	.....	.....
1/27/49	....	....	....	..	..	..	..	90.0	.....	7; 30	.....	.....

patient began to run a fever, rising to 100.8 F., which persisted for about a week. His general condition was fair. Because of secondary anemia, 500 cc. of blood were given Nov. 5, 1948.

Postoperative Course.—After the thoracoplasty the patient bled more than usual from the operative wound; his hemoglobin dropped to 8.5 gm., while his red blood cell count was reported to be 2,790,000. Four transfusions, each of 500 cc. of blood, were given to him, every other day, to combat the effects of hemorrhage.

On Nov. 24, 1948, he was returned to the tuberculosis service, where, on admission, he appeared to be pale and anxious; numerous petechiae and ecchymoses were scattered over his abdomen, arms, and legs as shown in the illustration. His spleen did not appear to be enlarged at that time. While under medical observation he complained of attacks of pain in the lumbar region and gross hematuria and nosebleeds developed. His pulse fluctuated between 80 and 100; blood pressure, between 148/98 and 98/58. He ran an occasional low-grade fever, rising to about 99.6 F. On Nov. 28, 1948, his hemoglobin was found to be 10 gm.; his red blood cell count was 3,210,000. The Leede-Rumpel hyperplasia of the granular cells with a 7% eosinophlia. The megakaryocytes were increased in number, but no blood platelet formation was noted. It was felt that findings in the bone marrow were compatible with a diagnosis of allergic thrombopenic purpura, probably due to streptomycin. The patient was empirically given vitamin K, crude liver extract, rutin, and occasional injections of meperidine (demerol®) hydrochloride for pain; but there was no improvement in his condition. Numerous petechiae and ecchymoses continued to develop. On Nov. 30, 1948, transfusions of citrated blood varying in amount from 250 cc. to 500 cc. each were started. These were given every other day for two weeks; because of no definite improvement, 10 daily transfusions were then given. About Dec. 18, 1948, the interval between transfusions was increased to three days, and they were finally discontinued on Dec. 30, 1948. Because of an allergic reaction, antihistamines were administered to the patient at the same time.

With this treatment, the patient improved gradually. His hemorrhages decreased in amount and became less frequent; the petechiae and ecchymoses subsided. The Leede-Rumpel phenomenon became less positive, and on Jan. 11, 1949, it was es-

sentially normal. On Dec. 28, 1948, the spleen had appeared to be somewhat enlarged for the first time and it remained definitely palpable for a few weeks. The patient's hemoglobin value and red blood cell count increased gradually, showing a tendency to become stable without the help of transfusions. Blood platelets increased gradually and were reported to be 32,000 per cubic millimeter on Dec. 15, 1948; 58,000 on Jan. 16, 1949, and about 90,000 at the beginning of February, 1949. Details of the laboratory findings are given in the Table. It was the impression of the medical staff that the patient had a thrombopenic purpura, probably caused by streptomycin. A splenectomy was considered; but in view of the progressive although slow improvement in the patient's condition, the decrease in the amount of bleeding, the increase in blood platelets, and the apparently allergic type of purpura it was felt that a splenectomy was not indicated, especially in view of the preceding two major operations.

During the patient's last examination at Billings Veterans Administration Hospital on Feb. 2, 1949, only a few small petechiae were noted on his forehead, while his spleen showed evidence of a decrease in size.

The patient left the hospital against medical advice on Feb. 2, 1949. He was seen as a follow-up patient on June 22, 1949, at Hines (Ill.) Veterans Administration Hospital, where no findings of purpura were noted during the examination.

COMMENT

Thrombopenic purpura developed in this patient following the administration of 25 gm. of streptomycin. No other drug definitely known to have a toxic effect on blood platelets was given to the patient. A significant factor might have been the sensitization of the patient by the administration of 2 gm. of streptomycin during April, 1947. Whether the two major operations performed on the patient on Oct. 28, 1948, and Nov. 15, 1948, made him more susceptible to the effect of streptomycin is conjectural. It is interesting to note that the amount of streptomycin administered to the patient before purpura developed was relatively small. In the cases reported by Feld, Deyke, and Wallace blood dyscrasia began to manifest itself after the administration of 70 to 80 gm. of streptomycin. The bone marrow findings were suggestive of an allergic type of purpura.

SUMMARY

A case of thrombopenic purpura is reported in a patient affected with quiescent pulmonary tuberculosis and tuberculous empyema. He was treated with decortication, a five-rib thoracoplasty, and 25 gm. of streptomycin. It is felt that this case of purpura hemorrhagica was most probably precipitated by the streptomycin.

ADDENDUM

The patient was last seen at the Fort Wayne (Ind.) Veterans Administration Hospital between Jan. 22, 1951, and Feb. 9, 1951. His general condition was very good. Scattered bluish ecchymoses on both arms and legs with a few petechiae were noted. The red blood cell count was 5,460,000, with a hemoglobin value of 15 gm. The white blood cell count was 14,520, with 78% polymorphonuclear leukocytes and 20% lymphocytes. The blood platelets numbered 94,000. The bleeding time was 15 minutes and the coagulation time (Lee-White) was 16 minutes. There was only slight clot retraction at the end of five hours. The prothrombin time was 18 seconds. The Leeds-Rumpel phenomenon was positive.

FIBRINOUS BRONCHITIS

REPORT OF CASE

John A. Callahan, Boston

Fibrinous bronchitis has been recognized as a disease entity for many years, probably because of its outstanding characteristic, the expectoration of bronchial casts by the patient. It was known to Galen, who considered the casts to be blood vessels expectorated from the lung. It was not until 1750 that Bussiere established that the casts were bronchial secretions when he demonstrated a cast in situ at autopsy. Lebert, in 1869, collected all the cases in the literature up to that time, a total of 44 cases. Bettman collected 145 cases from 1869 to 1902.[1] Walker found 31 cases reported from 1900 to 1920.[2] Since 1920 there have been about 26 cases reported, bringing the total reported cases to between 180 and 200. It is the purpose of this report to record a case which presented some interesting features.

REPORT OF A CASE*

A Negro woman, 54, was admitted to the Massachusetts Memorial Hospitals on Oct. 16, 1950, complaining of difficult breathing and cough productive of white, branch-like sputum of three months' duration. Three and one-half years ago the patient had had an episode of chest pain, which was aggravated by breathing and coughing and accompanied by fever. These symptoms disappeared in a week or two but have returned since, to a lesser degree, with upper respiratory infections. Over a period of seven months she lost 80 to 100 lb. (36.3 to 45.4 kg.), and complained of dizziness and drenching night sweats. Eight months prior to the present illness swelling and pain developed in the calf muscles of the left leg. Nine days later she noted recurrence of left pleuritic chest pain and cough productive of white "ropy" sputum.

On Feb. 26, 1950, she was admitted to another hospital with a diagnosis of pulmonary embolization and infarction (although there was no roentgenographic confirmation), deep thrombophlebitis of the left leg, bronchitis, and possible bronchopneumonia.

Three days after discharge she sustained a superficial injury with some bruising of the face and flank on the right side and the right leg. She became dyspneic again and was readmitted to the same hospital on April 5, 1950. The changes in physical examination at this time included slight distension of the neck veins but no hepatojugular reflex. The chest showed signs of diminished tactile and vocal fremitus with inspiratory crackling rales at the right base. Pulmonic second sound was louder than aortic second sound, but the examination of the heart was otherwise unchanged. There was tenderness of the right flank, and ecchymosis of the right leg was present. Laboratory data at this time revealed hemoglobin 10 Gm., leucocytes 8,600, and sedimentation rate 5 mm. in one hour. Two green reactions were obtained in tests of the urine for sugar. Blood culture yielded no growth. Gastric washings injected into a guinea pig in February were reported as negative for tuberculosis. Electrocardiogram showed sinoauricular tachycardia and incomplete auriculoventricular block. She was discharged on April 10, 1950, improved, with diagnoses of arteriosclerotic heart disease, cardiac enlargement, sinoauricular tachycardia, early mild cardiac decompensation, and possible diabetes mellitus.

After discharge she felt weak, had pains in her right chest and cough, which was productive of a moderate amount of white

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* From the Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals.

1. Bettman, M.: Report of a Case of Fibrinous Bronchitis, with a Review of All Cases in the Literature, Am. J. M. Sc. **123**: 304, 1902.
2. Walker, I. C.: Two Cases of Fibrinous Bronchitis, with a Review of the Literature, Am. J. M. Sc. **159**: 825, 1920.

foamy sputum, but no hemoptysis. These symptoms continued with no increase in severity and with few remissions until about three months before the present admission. Early in August, 1950, she noted the onset of dyspnea, severer than usual, wheezing localized to the right anterior superior portion of the chest, and violent coughing with blueness of the face. After several minutes of coughing, she expectorated a "white branch or tree-like thing" and felt much relieved. After expectoration, she felt a hollowness in the right side of her chest. She continued to have these episodes of dyspnea and cough productive of casts almost every day before admission. She reported that she coughed up between four and six casts each day, that some of them were tipped with blood, and that they were most often expectorated shortly after waking in the morning or about midnight. She was seen by the Home Medical Service of the Massachusetts Memorial Hospitals on Oct. 12, 1950, and admitted to the hospital.

Her past history was noncontributory. Her family history revealed a half sister had died of tuberculosis 15 years ago, but the patient denies any but the most casual contact with her. The patient's husband was said to have "a spot on the lung," but investigation in 1948 revealed pulmonary fibrosis and bronchiectasis, with guinea pig cultures negative for tuberculosis.

The patient was an obese Negro woman; she was able to sit up in bed, was breathing with some difficulty and coughing occasionally, but was in no acute distress. Her temperature was 99 F.; pulse, 100 per minute; respirations, 25, and blood pressure 138/88. The skin showed no scaling, eruptions, or abnormal pigmentation. Examination of the head revealed no abnormalities. A nontender lymph node, 1 cm., was palpable in the left jugulodigastric region. The anteroposterior diameter of the chest was increased. Respiratory expansion of the two sides of the chest was equal. Respirations were deep and somewhat labored. The apex impulse was not palpable. The left border of cardiac dullness was 2 cm. beyond the midclavicular line. The rhythm was regular except for occasional extrasystolic beats. A grade one systolic murmur was heard in the fourth intercostal space to the left of the sternum. Pulmonic second sound was louder than aortic second sound. There was prolongation of expiratory breath sounds, slightly diminished resonance, and moist rales over the lower third of the right chest posteriorly. Diaphragmatic excursion was equal bilaterally, 2-3 cm. Vocal and tactile fremitus were unaltered. Examination of the abdomen revealed an obese abdominal wall, one right upper quadrant and one midline hypogastric scar, vague tenderness but no spasm in the right upper quadrant, and no organs or masses palpable. The anus was constricted and would not admit the examining finger. Pelvic and neurologic examinations were normal. The extremities showed 1 + pitting pretibial edema and a nontender thrombosed vein in the left calf posteriorly.

Bronchial casts.

Pathologic description of the casts was as follows: Specimen consists of three "bronchial casts" (fixed in Zenker's solution) apparently having arisen from main stem bronchi and the primary division thereof (figure). Each cast measures approximately 4 cm. in length and 1.0 to 0.4 cm. in diameter. Cross section reveals fine cystic structure. Microscopic study indicates that sections of the casts are composed of mucus, fibrin, albuminous precipitate, scattered cells (some well-preserved and others degenerated and necrotic), and interspersed vacuoles representing entrapped air. No bacterial colonies or tumor cells were noted.

On admission, the hematocrit was 53 (Wintrobe), and the hemoglobin 17 Gm. Other laboratory studies were normal, but the roentgenogram of the chest showed enlargement of the right auricle, atelectasis at the right base, pulmonary congestion, and a cardiac configuration consistent with a small pericardial effusion. Shortly after admission, the temperature became elevated to 103.4 F. rectally, and she had dyspnea, tachycardia, and pain in the right shoulder. At this time venous pressure was 220 mm. (citrate), and arm to tongue circulation time was 38 seconds (dehydrocholic acid [decholin®]).

On the second hospital day her cough diminished, although small casts were still being expectorated. The blood pressure fell to 88/72, and the pulse rose to 110. The right border of cardiac dullness was found to be 5 cm. to the right of the midsternal line. The left border of cardiac dullness was 2 cm. to the left of the point of maximal cardiac impulse. There was no increase in venous distention, and the lungs were clear to auscultation and percussion. Fluoroscopy at this time revealed a small pericardial effusion. The leucocyte count rose from 7,700 to 13,900, and the electrocardiogram showed a P-R interval of 0.24 seconds and right ventricular strain.

The patient became asymptomatic on the fourth hospital day and expectorated no more casts during her hospital stay. Except for transient laryngitis, which responded quickly to symptomatic treatment, and temperature elevations every third or fourth day to 100 or 101 F., she remained asymptomatic.

Results of acid-fast studies by sputum smear, throat smear, smear of bronchoscopic specimen, and repeated gastric washings were negative. An intradermal first strength purified protein derivative test was normal, while the result of second strength was strongly positive at 24 and 48 hours. Repeated sputum cultures grew beta hemolytic Streptococcus, alpha hemolytic Streptococcus, Hemophilus influenzae, Micrococus pharyngis sicca, Neisseria flava and Micrococus catarrhalis, and, on one occasion, Escherichia coli. Corynebacterium diphtheriae was not seen. After the initial rise, the leucocyte count returned to normal but revealed a progressively increasing eosinophilia, reaching 17% on one occasion, which persisted until shortly before discharge. The result of an intradermal test (Bachman) with trichina extract was negative. Bronchoscopy was performed on the 14th hospital day. No gross lesions or casts were seen. All bronchial orifices were well visualized. A small amount of thin colorless secretion was seen issuing from the right main stem bronchus. Acid-fast smears and results of Papanicolaou studies on this material were negative. Vital capacity studies at regular intervals were consistently between 2.3 and 2.6 l. Venous pressure toward the end of the hospital stay was 205 mm. (citrate), and circulation time was 24 seconds (dehydrocholic acid). The patient was digitalized slowly and adjusted to a maintenance dose of digitoxin. She was discharged asymptomatic, but febrile, on the 32nd hospital day.

COMMENT

Fibrinous bronchitis is usually described as a rare disease, but its true rarity is somewhat in doubt. Walker, in 1920, knew of three unreported cases in addition to the two he reported, and suggested that "a more careful examination of the sputum of patients with bronchitis and the like, would probably result in a still greater yield of cases of fibrinous bronchitis."[3] The casts are expectorated as white masses in the sputum, which when floated in water can be made to unravel and show their branched form. They may be small portions of a larger cast or may

3. (*a*) Lord F. T.: Diseases of the Bronchi, Lungs and Pleura, ed. 2, Philadelphia, Lea & Febiger, 1925. (*b*) West, S.: Diseases of the Organs of Respiration, London, Griffin & Company, Ltd., 1902.

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be almost exact reproductions of the bronchial tree.[8] They are composed of fibrin and mucin, and at one time they were classified according to the predominating substance. This classification is no longer considered useful. The casts may contain desquamated epithelial cells, bacteria, red blood cells on the surface although rarely in the substance, and, according to some authors, Charcot-Leyden crystals and eosinophils.[4] The large portions of the cast may be hollow, although they usually are filled with mucus and do not admit air, while the smaller terminal portions are uniformly solid and may resemble Curschmann's spirals. The bacteria that have been isolated from the casts include streptococci, staphylococci, pneumococci, Corynebacterium diphtheriae, Klebsiella pneumoniae, Mycobacterium tuberculosis, and Hemophilus influenzae.[5]

Walker expressed the opinion that fibrinous bronchitis should be considered a primary disease and that casts formed during the course of other diseases should be considered symptomatic of those diseases.[2] Most authors believe, however, that primary and secondary forms exist and that acute and chronic courses are seen in both forms.[6] It has been reported in association with other pulmonary diseases such as tuberculosis, asthma, bronchial compression due to tumor, to aneurysm, to enlarged bronchial glands, fungus infection, chronic passive congestion or heart disease, pulmonary edema, and conditions after exposure to noxious inhalants such as live steam, smoke, and ammonia. General constitutional disturbances with which it has been reported include typhoid fever, scarlet fever, smallpox, rheumatism, influenza, erysipelas, diphtheria, pemphigus, impetigo, and herpes zoster. It is reported to be more frequent in males and commonest between the ages of 10 and 30 years.

There is no specific etiology known. Many different bacteria have been isolated, as mentioned before, but none of these has been found consistently. Rakower believes that a constitutional predisposition exists and that the disease is produced by a precipitating factor such as bacterial infection or mechanical or physiochemical influences.[7] Weber [6f] observed a case in association with exophthalmic goiter which improved when the thyrotoxic disease did. The disease has been compared to mucous colitis as an upset of the autonomic and endocrine systems. Roth, reporting in 1938, felt the disease to be related to allergic reactions and histamine. He treated one patient successfully with torantil® (a histaminase preparation) intramuscularly. After the disappearance of symptoms, histamine was given subcutaneously, and relapse followed. The relapse was treated successfully with torantil.[8,8] This report is difficult to evaluate in the light of a report by Feinberg in 1946, which stated that all histaminase preparations available to the date of his publication were inactive in the treatment of allergic states or diseases in man.[9] Keizer, in 1949, thought the disease resembled asthma and suggested the use of antihistaminic drugs for treatment, although he did not use them in his case.[4a]

There are three cardinal symptoms of the disorder: dyspnea, cough, and expectoration of casts. There is great variation in the severity of these symptoms from expectoration of casts after hawking to suffocating dyspnea and violent paroxysmal coughing. In some cases the casts cannot be coughed up, and the patient dies of asphyxia. There is usually some degree of fever, which however is in no way characteristic. Chills may precede the paroxysm of dyspnea, and hemoptysis of varying amount may follow. Acute cases are usually marked by severe dyspnea and sometimes by deep cyanosis. The severity of symptoms may depend on the extent of bronchial involvement. The chronic form is much more frequent. The expectoration of casts may occur at intervals over many years and during the periods of active disease one to ten casts may be produced daily.[10]

The physical signs are not characteristic and the diagnosis must be made on the basis of casts found in the sputum.[5b] Rales and diminution of breath sounds and resonance may be heard over an area where casts are forming. Any type of rales may be heard, including one perhaps more characteristic than others, a rough, snapping, bronchial type believed to be caused by flapping of the ends of the casts in the bronchi and to which the French have given the name *bruit de drapeau*.[11] Other physical signs due to associated disease or to complications such as bronchostenosis, focal or massive atelectasis may be observed.[12] Chronic emphysema is often seen in cases of long standing. Considerable loss of weight may occur without any other explanation. Night sweats have been reported in cases in which no acid-fast infection could be demonstrated.[1] Roentgenographic findings are also not specific. They are increased hilar density and increased bronchovascular markings.[13] Walker described mottling of the lung fields in one case.[2]

Prognosis in cases other than those in which the patient dies of asphyxia is largely dependent on the associated diseases. In uncomplicated, primary cases in which casts are expectorated periodically without great difficulty, the patient may live normally between paroxysms. Many cases clear up completely without recurrence.[14] Those acute cases resulting in death from asphyxia are relatively uncommon, although Johnstone reported one in 1945.[10c]

The treatment of this disease has been varied and has included inhalations of steam, calcium hydroxide solution (lime water) spray, dilute sodium hydroxide with

4. (*a*) Keizer, D. P. R.: Bronchitis mucinosa fibrinosa, Nederl. tijdschr. geneesk. **93**: 3729, 1949. (*b*) Mercia, F. W.: Acute Fibrinous Bronchitis with Massive Atelectasis, Ohio M. J. **46**: 1079, 1950. (*c*) West.[3b]

5. (*a*) Keizer.[4a] (*b*) Lord.[3a] (*c*) Meyer, A.: Ueber Bronchitis fibrinosa acuta, Klin. Wchnschr. **16**: 1126, 1936. (*d*) West.[3b]

6. (*a*) Bettman.[1] (*b*) Lord.[3a] (*c*) Meyer.[5c] (*d*) Mulligan, P. B., and Spencer, R. D.: Chronic Fibrinous Bronchitis as a Symptom of Mediastinal Compression, J. A. M. A. **82**: 791 (March 8) 1924. (*e*) Shoyer, A. F.: Fibrinous Bronchitis, Brit. M. J. **2**: 1035, 1906. (*f*) Weber, H.: Exophthalmic Goiter and Fibrinous Bronchitis, Med. Klin. **17**: 1143, 1921; abstracted, J. A. M. A. **77**: 1932 (Sept. 18) 1921. (*g*) West.[3b]

7. Rakower, J.: Atelectasie massive au cours de la bronchite pseudomembraneuse primitive, Presse méd. **46**: 1116, 1938.

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9. Feinberg, S. M.: Histamine and Antihistaminic Agents: Their Experimental and Therapeutic Status, J. A. M. A. **132**: 702 (Nov. 23) 1946.

10. (*a*) Bettman.[1] (*b*) Huber, J. P.; Chevallier, and Gerbay: Angine à monocytes et trachéo-bronchite pseudo-membraneuse, Ann. otolaryng. **63**: 784, 1948. (*c*) Johnstone, D. F.: Acute Plastic Bronchitis (with Case Report), Guy's Hosp. Gaz. **59**: 2, 1945. (*d*) Lawhead, N. R.: Acute Fibrinous Bronchitis: Report of a Case, J. Michigan M. Soc. **20**: 14, 1921. (*e*) Lord.[3a] (*f*) Marshall, W. H.: Acute Fibrinous Bronchitis, ibid. **19**: 552, 1920. (*g*) West.[3b]

11. Lord.[3a] Marshall.[10f] West.[3b]

12. (*a*) Malamud, T., and Lisman, A.: Atelectasia aguda de un lóbulo pulmonar en una bronquitis pseudo membranosa frusta, Prensa méd. argent. **33**: 2362, 1946. (*b*) Mercia.[4b] (*c*) Perlstein, R. N.: A Case of Fibrinous Bronchitis Complicated by Massive Atelectasis, Am. Rev. Tuberc. **22**: 82, 1930. (*d*) Rakower.[7]

13. Rodenbaugh, F. H.: Fibrinous Bronchitis, Am. J. Roentgenol. **10**: 843, 1923.

14. Bettman.[1] Walker.[2] West.[3b]

calcium hydroxide solution, potassium iodide, mild mercurous chloride (calomel), lead acetate, sulfur, nitrous ether (sweet spirit of nitre), phlebotomy, ipecac, antimony and other emetic measures, sulfapyridine, penicillin, torantil,* manual compression of the chest during expiration, pneumothorax, bronchoscopic removal of the cast, and tracheotomy.[15]

SUMMARY

A case of fibrinous bronchitis is reported in a woman who had had thrombophlebitis of the deep calf veins and pulmonary infarction in the past. The main features of the disease are reviewed, and attention is directed to the fact that this form of bronchitis is perhaps commoner than is generally supposed. It is overlooked, because the sputum of patients with bronchitis is not always examined in such a way as to result in detection of the casts.

80 E. Concord St.

15. Bettman,[a] Christian, H. A.: Fibrinous Bronchitis, M. Clin. North America **2**: 1255, 1919. Huber.[10b] Johnstone.[36c] Keizer.[4a] Lawhead.[10d] Lord.[5a] Mercia.[4b] Meyer.[3c] Mulligan and Spencer.[6d] Oliver, T.: Remarks on Plastic or Croupous Bronchitis, Brit. M. J. **2**: 69, 1899. Roth.[5] Seiler, S.: Ueber Bronchitis plastic (mit Mitteilung eines durch Kollapstherapie geheilten Falles), Schweiz. med. Wchnschr. **72**: 86, 1942. Walker.[3] Weber.[6f] West.[2b]

RETICULUM CELL SARCOMA OF MESENTERY

CASE WITH PRONOUNCED FEBRILE MANIFESTATIONS

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and
Benjamin L. Schulman, M.D., Pittsburgh

Jackson and Parker [1] found that pronounced fever was rare in reticulum cell sarcoma unless associated with sepsis. Gall and Mallory [2] noted that fever of 101 F. or higher occurred at some time during the course of the disease in all the malignant lymphomas, but was relatively uncommon in clasmatocytic (25%) and stem cell (29%) lymphomas.

Gall and Mallory,[2] in offering a different classification of malignant lymphomas in a study of 618 cases, divided the specimens into seven categories. The "reticulum cell sarcomas" were divided into two types: (1) stem cell lymphomas (tumors composed of highly undifferentiated, supposedly pluripotential cells, called stem cells) and (2) clasmatocytic lymphomas (tumors made up of fairly well differentiated cells, simulating normal clasmatocytes or monocytes, the cells being smaller than stem cells, but distinctly larger than lymphocytes). The other five categories of malignant lymphoma are (3) lymphoblastic lymphoma, (4) lymphocytic lymphoma, (5) Hodgkins lymphoma, (6) Hodgkins sarcoma, and (7) follicular lymphoma. Other classifications have been given for malignant lymphomas [3] and reticulum cell sarcomas.[4]

Gall and Mallory [2] studied a group of 70 initially localized malignant lymphomas, of which 32 were "reticulum cell sarcomas." Three of these were found in the abdominal lymph nodes, one being a stem cell lymphoma, its duration one to two years, and its ultimate distribution generalized. Two were clasmatocytic lymphomas of the abdominal lymph nodes. The first was of 0.5 years' duration, the ultimate distribution generalized, the diagnosis being made at autopsy; the other was of 1.1 years' duration, and the ultimate distribution local. Of the three cases, only one was of local ultimate distribution. Edling [4b] found that a marked characteristic of reticulum cell sarcomas was their pronounced tendency to become generalized.

The purpose of this report is to record a case of reticulum cell sarcoma of the mesentery, in which high septic fever was a pronounced manifestation, and whose ultimate distribution was apparently local.

REPORT OF A CASE

An Oriental Moslem man, age 35, was admitted to the hospital on Aug. 31, 1948, with a chief complaint of fever. The present acute illness had started approximately two months prior to admission. At that time, symptoms were anorexia, nausea, and mild diarrhea. The patient was treated by his physician, with complete abatement of symptoms in a few days. Two weeks prior to admission he developed a fever of 101 F., complained of sore throat, which on examination by his physician was reported as injected. At that time, he was given sulfathiazole; then he received intramuscularly 300,000 units of penicillin daily. In spite of the treatment, the temperature was 100.6 F. rising to 103 F. on the evening of admission. He complained of being hot and weak. He had no pain, and there was no apparent weight loss or gastrointestinal complaints.

The past history disclosed the following: During childhood, while in India, an incision and drainage of the glands on the right side of the neck had been done. There were no complications resulting. He had no other operations or illnesses prior to the onset of his present illness. He had no previous gastrointestinal disease or fever. He denied syphilis, malaria, and all diseases endemic to his native country, India.

When seen for the first time, he was acutely ill and weak. The temperature was 100.6 F., pulse 108, respirations 22 per minute, and blood pressure 102 systolic and 70 diastolic (mm. Hg.). Slight pallor of the lips was noted, and there was no apparent weight loss. Examination of the head was normal. The eye grounds showed no exudates, hemorrhage, or papilledema. The conjunctivae showed no icterus. The ears and nose were not remarkable. The teeth were normal, as was the throat. There was a small healed scar over the right side of the neck in the area of the anterior cervical glands. The anterior and posterior cervical glands were not tender or palpable. The lungs were resonant to percussion, and no rales were found. The heart tones were of good quality, and a sinus tachycardia was present.

The abdomen, which was not distended or rigid, was tympanitic on percussion and normal on auscultation. The liver, spleen, and kidneys were not tender or palpable. A mass about orange-size was palpable just to the left of the umbilicus. The mass was firm, round, and neither tender nor movable. There was no pulsation felt or abnormal sound heard. The genitalia were normal. The extremities were warm; the pulses were easily palpable. The axillary and inguinal glands were not tender or palpable. Rectal examination was normal.

The urinalysis at the time of admission revealed no significant abnormalities. The red blood count was 3,950,000; hemoglobin 11 Gm.; the white blood count 12,050; a differential count showed neutrophils 65%; lymphocytes 32%; eosinophils 2%, and basophils 1%. A roentgenogram of the patient's chest was

Dr. W. J. Winter, Assistant Chief of the Pathology Service, Veterans Administration Hospital, Aspinwall, Pa., gave suggestions and advice.

1. Jackson, H., Jr., and Parker, F., Jr.: Hodgkins Disease and Allied Disorders, New York, Oxford University Press, 1947, pp. 113-132.

2. Gall, E. A., and Mallory, T. B.: Malignant Lymphoma: A Clinico-Pathological Survey of 618 Cases, Am. J. Path. **18**: 381, 1942.

3. Callender, G. R.: Tumors and Tumor-like Conditions of the Lymphocyte, the Myelocyte, the Erythrocyte and the Reticulum Cell, Am. J. Path. **10**: 443, 1934.

4. (*a*) Warren, S., and Picena, J. P.: Reticulum Cell Sarcoma of Lymph Nodes, Am. J. Path. **17**: 385, 1941. (*b*) Edling, L.: Contribution to the Pathology and Clinical Picture of Reticulum-Cell Sarcoma, Radiology **30**: 19, 1938.

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reported as follows: The heart and great vessels are normal. The apices are clear; there is no pleural effusion. The hilar glands are increased in size. There is no evidence of tuberculosis. The electrocardiogram on admission revealed a sinus tachycardia, rate 120. A blood smear was taken for malaria, and agglutination tests were performed with typhoid O and H antigens, paratyphoid A and B, Proteus O X_{19}, and Brucella abortus.

Penicillin was administered intramuscularly, 300,000 units twice daily, and quinine sulfate, 0.33 Gm., was given orally four times daily as the temperature began to rise.

On the second hospital day the temperature was 100 F.; the patient had no complaints other than those of fever and weakness. He continued to have daily elevations of temperature in spite of the treatment he was receiving (fig. 1). On the fifth hospital day, intramuscular administration of penicillin and quinine sulfate taken orally were discontinued. The patient was given sodium sulfathiazole, 4 Gm. at the start and 1 Gm. every

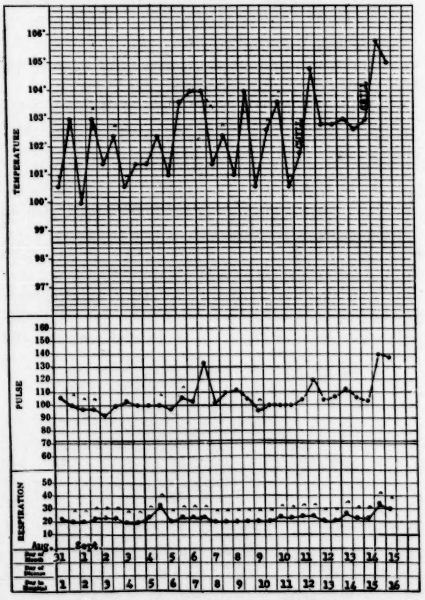

Fig. 1.—Temperature curve showing pronounced fever

four hours. A blood cell count done at this time showed red blood cells 3,430,000, hemoglobin 9.3 Gm., and white blood cells 9,500. Differential count showed neutrophils 85%; lymphocytes 13%; eosinophils 1%, and basophiles 1%. Urine was normal. A malaria smear showed no plasmodia. A throat smear was negative. Sputum cultures for tubercle bacilli were negative. Stool examinations revealed no ova or cysts. Agglutination tests with typhoid O and H antigens, paratyphoid A and B, Proteus O X_{19}, and Brucella abortus gave negative results. Heterophil antibody titer was 1:7. A blood culture taken on the first hospital day showed no growth. The result of the spinal fluid Kolmer test was negative. There was no increase in pressure, cells, sugar, or protein. A roentgenogram of the patient's chest was reported as follows: Since the last examination, there has been no change in the appearance of the hilar glands. An area of right hilar density may represent a small area of pneumonic consolidation or could represent enlarged hilar glands. There is no evidence of tuberculosis.

On the ninth hospital day the temperature was 101 F., and the patient felt improved. A pallor developed, and weakness continued. That evening the temperature rose to 104 F., dropping the next morning to 100.6 F. On the eleventh hospital day the temperature was 103.8 F., and the patient refused to eat. He had anorexia but no vomiting. On the twelfth hospital day, the patient had a chill, and temperature rose to 104.8 F. The following day the temperature returned to 102.8 F. A malarial smear taken was negative for plasmodia. On reexamination of the abdomen, the liver and spleen were not tender or palpable. The mass remained the same size, was firm and round, and had become tender on pressure. It was slightly movable. There was no distention, and normal peristalsis was present. The patient had had a bowel movement daily except on the eighth hospital day. A transfusion of 500 cc. of whole blood was given. Because of the spiking nature of the temperature, the possibility of an inflammatory involvement of the mass was considered. Surgical consultation indicated a laparotomy essential.

On the fourteenth hospital day the temperature remained at 102.8 F. The patient was started on streptomycin, 0.25 Gm. every six hours. He was given 500 cc. whole blood and parenteral fluids. On the fifteenth hospital day a laprotomy was performed. A large tumor infiltrating the mesentery of the small intestine was found. A few retroperitoneal nodes were enlarged; the liver and spleen were not enlarged. The large mesenteric tumor, associ-

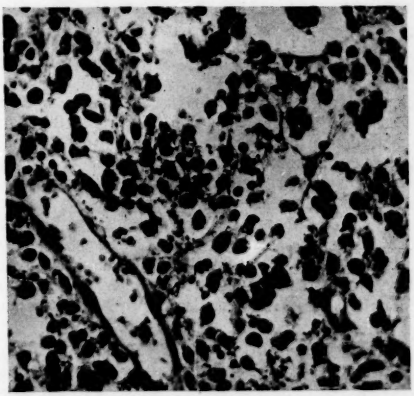

Fig. 2.—Photomicrograph of the mesenteric tumor, clasmatocytic lymphoma. The nuclei exhibit a pronounced degree of variation and are eccentric (× 275).

ated with considerable suppuration, necessitated removal of 31 inches (78.74 cm.) of small intestine. Immediately postoperatively the patient's temperature was 103 F. He was given a transfusion of 500 cc. whole blood and parenteral fluids. On the evening of the fifteenth hospital day, the temperature began to rise, and the patient had a severe chill. The temperature rose to 105.8 F., dropping to 105 F. on the sixteenth day (fig. 1). The patient became cold and clammy, the pulse weak, and he died at 12:45 a. m. of the sixteenth hospital day. An autopsy was not performed.

Gross description was as follows: Eighty-two cm. of small bowel with mesentery attached is 32 mm. in average diameter. The mesentery is altered by pronounced thickening near the base which averages 3.5 cm. Four other pieces of mesentery received separately measure from 3 to 12 cm. across. The thickened portion consists of smooth, glistening, grayish white tissue, extensively infiltrating and replacing the adipose tissue. Localized hemorrhagic nodules about 1 cm. across are present in the subserosal portion. Discrete lymph nodes are not present in the mass, which has obliterated everything in the periphery of the mass. A very occasional fatty and hemorrhagic nodule is observed. The resected portion of the bowel has an unaltered wall and a pale intact mucosa, having circular folds characteristic of the lower jejunum. The lumen contains brownish black material resembling the bowel content of a patient receiving iron medication.

Microscopic description revealed the following: Sections of the mesenteric lymph nodes are completely replaced by a poorly differentiated tumor composed of cells that are irregular in outline (fig. 2). The cells are approximately 14 to 24 μ in diameter. The cytoplasm is more abundant than is usually seen in the stem cell type. The nuclei are eccentric in position, some being round, oval, or horseshoe-shaped. A fine network of chromatin is present. The cells are supported on fine reticulum strands. Regions of necrosis are common, and growth adjacent to blood vessels is pronounced. Infiltration of the nerve trunks is marked on many of the sections.

SUMMARY

A case of reticulum cell sarcoma of the mesentery causing pronounced febrile manifestations is presented. The tumor was apparently localized to the abdominal lymph nodes, as no generalized involvement was found. It is suggested that the mesenteric lymph nodes are the causative site of origin of the tumor in this case.

Woodlawn Medical Center (Dr. Fein).

IMPROVED ANESTHESIA SCREEN

Frank Cole, M.D., Lincoln, Neb.

The usual anesthesia screen is almost without exception straight, that is, it consists of three sides of a rectangle. This is certainly the simplest and the most stable design; the result is the erection, some 20 in. above the operating table, of a rigid bar having the appearance of a straight line. The surgeon, who almost invariably places an assistant between himself and the anesthetist, desires that this bar be moved as far cephalad as possible. The anesthetist, who is at a loss to understand why even the patient's head must disappear from his view and reach during abdominal surgery, hopes to locate the screen as far caudad as possible. The result

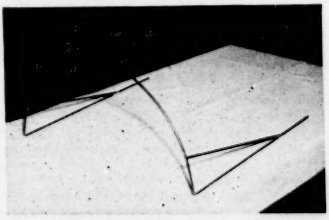

Fig. 1.—Semicircular anesthesia screen.

is that the screen generally is placed directly over the patient's eyes; it is often pushed back after the operation has been started.

It is the surgeon's arm and elbow and those of his assistant that require room at the head of the table; this room is needed only laterally. The anesthetist is anxious to be able to see and to reach the patient's head for change of position, suctioning, or tracheal intubation; the space he demands is located toward the midline of the table. With these two facts in mind, a new and better shape for the old "ether screen" becomes apparent, one in which the top horizontal bar has the contour, not of a straight line, but of either a curve, such as a semicircle, or two straight lines forming an angle. With this newer design, there will be room for the assistant's elbows at

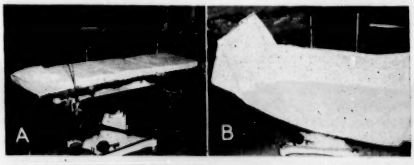

Fig. 2.—Improved screen attached to operating table (*A*) and with draping (*B*).

the side, while the anesthetist may have exposed for him the patient's entire head.

A semicircular screen has been constructed and has proved satisfactory in actual use. Draping is no more difficult than with the conventional anesthesia screen. The patient's entire head has been accessible to the anesthetist without his being required to reach under the drapes. In performance of laryngoscopy, the screen no longer impinges on the handle of the laryngoscope. Surgical assistants have been pleased to find as much room for their elbows as they could want.

The screen is shown in the accompanying illustrations (figs. 1, 2, and 3). It is obviously adjustable to any desired height, can be moved cephalad or caudad, and

Fig. 3.—Anesthesia screen during operation.

can be rotated as easily as the conventional screen (fig. 3*A*). It affords the assistant a greater degree of comfort, in that the corner no longer impinges on his arm. Since the new screen faces him in every position, it is no longer possible or necessary for the assistant to contaminate himself by having his elbow, upper arm, or shoulder behind the sterile screen while holding a retractor.

Veterans Administration Hospital

Chief, Department of Anesthesiology, United States Veterans Administration Hospital.

Reviewed by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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ARM REST FOR THE SURGICAL ASSISTANT

Frank Cole, M.D., Lincoln, Neb.

The surgical assistant's practice of resting his forearm on the patient's chest has long been a source of contention between him and the anesthetist. It is not denied that he does want some means of support; it is indeed wearying to hold one's hand in a single position without rest for hours, particularly while holding a retractor. On the other hand, the anesthetist's objection is not without justification. The fact that the assistant's task is tiring does not warrant his transferring his burden to the patient, whose chest cannot be looked on as an inert and insensitive object. I have heard more than one patient under spinal anesthesia complain of the weight of the assistant's arm. Surely it requires a considerable effort for a patient, conscious or unconscious, to lift an assistant's forearm with each inspiration. In addition, heavy drapes, numerous instruments, and even the patient's own stomach have been found resting on his chest. All this must necessarily be reflected in his respiratory and circulatory patterns and often denies him a good anesthesia.

The weight imposed on the defenseless patient, which he is thus required to lift about 24 times each minute, was estimated by weighing my own forearm under simulated operating room conditions and was found to be 5 lb. My hand, as nearly as I could judge, weighed 3 lb., and my hand and wrist weighed 3½ lb. When the hand resting on the patient's chest is at the same time pulling on a retractor, the force the patient is required to overcome during inhalation may be considerably more than this.

Lifting five pounds a vertical distance of one-half inch 24 times a minute amounts to a work output of 300 foot pounds per hour, a tremendous load to be inflicted on the respiratory muscles of an unconscious patient, in whom the effect is not merely fatigue but dyspnea. During the course of a major surgical procedure, this may amount to an energy expenditure of more than 1,000

Fig. 1.—Photographs showing arm rest for surgical assistant.

foot pounds. For two tired assistants, one on either side of the table, these figures must of course be doubled. All this may easily be regarded as a form of respiratory obstruction.

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

I have constructed a device that will provide a rest for the assistant's arm and will allow the patient to breathe effortlessly (figs. 1 and 2). In addition, it may be used as a second instrument tray. The device has proved satisfactory in actual use. It has always been possible to

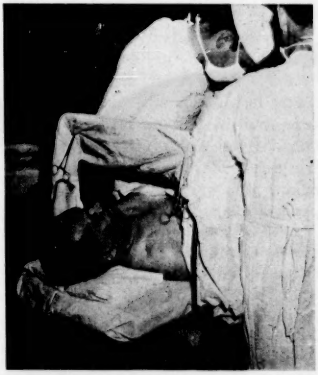

Fig. 2.—Photograph of arm rest in operating room.

obtain free space between the patient's chest in maximal inspiration and the arm rest; draping has not been more difficult. All surgical assistants who have tried it have been delighted with it. The device has been built in two forms. Both are easily adjustable to any height and to any position between the patient's shoulders and abdomen.

Veterans Administration Hospital.

Shortcoming in the Hospital Routine.—Generally speaking, the thing most desired by the newly puerperal woman is rest. Indeed, unless there have been complications this is likely to be her greatest need. Yet what does she get? She may obtain a good night's rest with the many benefits resulting from refreshing sleep, but then again she may not. Frequently those who cannot afford a private room—and they are in the majority—are returned to a ward or semiprivate area where others are in the process of rising. Sleep and rest, therefore, even with the aid of sedation, is brief and fitful. There is no prolonged refreshing slumber, nor is there likely to be, for whether the patient is in a ward or private room, her presence in a hospital today appears to be a matter of secondary importance. Secondary to obsolete but fixed hospital routine, secondary to the schedules of ward helpers, orderlies, nurses and doctors. At some absurd hour she is awakened. The technic used for this cruel procedure will, of course, vary. It may be a thermometer inserted into her mouth, a pitcher of ice water placed on her table or instructions to get washed and ready for breakfast, which commonly arrives an hour or two later. Any attempt to snatch a brief rest during the remainder of the day is likely to be interrupted by the vips, very important people such as her baby, the cleaning woman, the nurse, the doctor and others. I do not mean to be facetious in thus commenting upon the difficulty of obtaining rest in a hospital. I seriously believe this has become one of the most important and not too well recognized bugaboos of hospital life. I believe it is an important factor in contributing to the emotional upset and tears so frequently noted amongst puerperal women. Too often it marks the beginning of the well recognized fatigue syndrome so commonly observed in new mothers.—Norman F. Miller, Shortcomings in Puerperal Care, *The Journal of the Iowa State Medical Society*, July, 1951.

MYASTHENIA GRAVIS IN A MOTHER AND HER NEWBORN SON

George E. McKeever, M.D., Detroit

Myasthenia gravis is a disease that lends itself well to study. The history and physical findings are well defined, although variable. Almost absolute proof of the diagnosis is available in the test dose of neostigmine (prostigmin*). As a result, many articles are to be found in the recent literature. Numerous series of cases have been available for the study of such particular manifestations of the disease as the ocular and the bulbar. Certain aspects, however, are sufficiently rare to warrant case reports. Among these are cases of myasthenia gravis complicating pregnancy and congenital myasthenia gravis. Of the latter, a total of 10 cases has been reported, the first in 1942.[1a] Of the 10 cases, the congenital nature of the disease was determined by retrospect in four. In the other six cases the diagnosis was made in the neonatal period. In this report the seventh known case of myasthenia gravis occurring in a newborn child of a myasthenic mother is described.

REPORT OF CASES

CASE 1.—The mother, Mrs. L. B., a 32-year-old Negro graduate nurse, entered Harper Hospital Dec. 11, 1949, complaining of weakness and weight loss associated with pregnancy. The patient had been well until August, 1948, when she noticed that she was unable to squeeze clothespins when hanging up clothes. In November, 1948, she observed that she could not fasten the buttons on her nursing uniform or tie her shoestrings. The disability was intermittent and variable from day to day. She could not manipulate her fingers in the morning when coming on duty, but after being on duty and busy she had no difficulty. She was unable to carve meat because of "stiffness of the fingers." In January, 1949, the patient was, for the first time, unable to raise her hands to comb her hair. Early in March, 1949, she experienced weakness of the right leg while attempting to board a bus; it was of such severity that she was unable to climb all the steps into the bus. She backed off the steps and went to the emergency room of a local hospital, where she was seen in the neurosurgical department. No diagnosis was made other than a definite weakness of the right leg. After this examination the patient developed blurring of vision. She was admitted to the above-mentioned hospital on the neurosurgical service. After being studied for seven days she was discharged with no definite diagnosis; multiple sclerosis was suspected. The patient stated that she was helped by the bed rest. She returned to her occupation as a nurse during the first week in April, 1949. She was able to work until May, 1949, when the weakness of the right leg and blurring of vision recurred. She then consulted a private physician, whom she saw weekly during the months of May and June. In the latter part of June, 1949, she consulted her obstetrician because of suspected pregnancy. The diagnosis of pregnancy was confirmed. The last menstrual period was given as June 15, 1949. She had some nausea and vomiting of pregnancy during June. Physical examination was within normal limits except for the presence of multiple large and small uterine myomas. The date of confinement was estimated to be Feb. 22, 1950, because of the size of the uterus. The obstetrician was unaware of the complaint of weakness because it had disappeared. She remained at her job until Aug. 21, when she resigned because of abdominal pain that caused her to go to bed for one week. The cause of the pain is unknown. The patient continued to be free from weakness until the third week in November, 1949, the sixth month of pregnancy, when she noticed gradual loss of strength, had difficulty in climbing stairs, and ptosis of the left eyelid and diplopia developed. She became progressively weaker, with loss of appetite and weight. Chewing became difficult. No dysphagia was noted. During December the generalized weakness increased until the time of admission, Dec. 11, 1949.

Past History.—The patient was one of seven-month, premature, fraternal twins. She had come to Detroit with her family in 1926 from her place of birth, Port Limén, Costa Rica. She had always been healthy. The mother and father were both alive and well. The twin brother was well and on active duty with the navy. One brother had died at the age of 6 years of pneumonia. There was no history of weakness in any member of the family.

Physical Examination.—The patient was a thin Negro woman, appearing lethargic and chronically ill. There was slight ptosis of the left upper eyelid. The extraocular movements were normal. No pallor of the optic disks was noted. There was a perforation of the left tympanic membrane, with evidence of chronic otitis media. The mouth was normal except for copious amounts of a thick mucoid saliva. The patient was unable to swallow or expectorate the saliva, which drooled from her open mouth. The chest was normal except for evidence of weight loss. The lungs were clear to percussion and auscultation. The breasts were normal and full. The heart was of normal size, rate 90, rhythm regular. A faint systolic murmur was heard over the pulmonic area. Abdominal examination disclosed an enlargement of the uterus compatible with a six and one-half month pregnancy. Multiple uterine myomas were readily palpable through the abdominal wall. The extremities were normal except for evidence of weight loss. Neurological examination elicited normal findings in all respects except for generalized weakness and ptosis of the left eyelid. The weakness was so severe that she was unable to hold up her head. The hand grip was almost imperceptible. Inability to swallow was manifested by the copious salivary secretions that had to be wiped away from the tongue frequently. The face was masklike and sad. The patient was mentally clear.

Laboratory Data.—The red blood cell count was 3,930,000 per cubic millimeter and the hemoglobin was 10.7 gm. or 70%. Leukocytes numbered 9,700 per cubic millimeter, of which 80% were neutrophils, and 20% lymphocytes. Urinalysis and Kahn's test elicited normal findings. Blood type was B, Rh negative. Fasting blood sugar was .075 gm. per 100 cc. Nonoprotein nitrogen was 21 mg. per 100 cc.

Diagnosis.—A diagnosis of myasthenia gravis was suggested and the patient was given 1 mg. neostigmine methylsulfate intramuscularly. Within 15 min. there was a spectacular improvement in strength of facial expression and ability to swallow. The hand grip was notably stronger. There was also an increase in general strength and sense of well-being. The diagnosis of myasthenia gravis was established.

Hospital Course.—The patient was started on intramuscular neostigmine methylsulfate, 1 mg. before meals, supplemented by 15 mg. of neostigmine bromide as soon as she was able to swallow in response to the intramuscular neostigmine. By Dec. 22, the 12th hospital day, she had gone into a spontaneous remission and was subsequently carried on a dose of 15 mg. neostigmine bromide three times daily by mouth. There were minor variations in the daily dose. The maximum was 5 tablets, and the minimum was 1 tablet. Because of anemia and debility, the patient was given multiple blood transfusions. Her appetite, strength, and general condition improved steadily, and she had gained 21 lb. (9.5 kg.) by the time of delivery.

On Feb. 19, 1950, loss of muscular strength was noted. This was especially severe in the muscles of the jaw, manifested by inability to chew food. The relapse persisted for three days. On Feb. 22, 1950, there was an increase in strength and general sense of well-being. At noon the patient began to have half-minute labor pains every three minutes. She was transferred to the obstetrical floor, where vaginal examination disclosed an

From the Medical Department, Harper Hospital.

1. (*a*) Strickroot, F. L.; Schaeffer, R. L., and Bergo, H. L.: Myasthenia Gravis Occurring in an Infant Born of a Myasthenic Mother, J. A. M. A. **120**: 1207 (Dec. 12) 1942. (*b*) Wilson, A., and Stoner, H. B.: Myasthenia Gravis: A Consideration of Its Causation in a Study of 14 Cases, Quart. J. Med. **13**: 1, 1944.

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occiput posterior position of the fetus. A moderate amount of vaginal bleeding had been observed. It had been originally planned to deliver the infant from below. In view, however, of the posterior position of the fetus, the vaginal bleeding, the age of the patient and her primiparity, and the presence of multiple large uterine myomas, a decision was made to deliver the baby by Porro cesarean section. Under spinal anesthesia, the patient was delivered of a 6-lb. 10-oz. (3 kg.) male infant by Porro cesarean section at 8:30 p.m., Feb. 22, 1950. The operation was performed without incident. The patient's condition remained good until 7:30 a.m., Feb. 23, when the pulse became imperceptible, the blood pressure unobtainable, and perspiration profuse. The veins were collapsed. A venesection was performed, and the patient was given 1,000 cc. whole blood and 2,000 cc. of dextrose in water. She had been anuric. By 1:30 p.m. she was out of shock. During the period of shock, there was no evidence of muscular weakness. The patient received only 1 tablet of neostigmine bromide on Feb. 23. On Feb. 24 she began to have fever up to 100.4 F. With this elevation in temperature the patient developed ptosis of the left eyelid and weakness of the jaw muscles. She showed no weakness on Feb. 25, and was strong until Feb. 27 when she developed a chill with fever up to 101.3 F. Dysphagia was noted, but no other weakness. On March 1 profound generalized weakness developed in the patient which closely resembled that present on admission 12 weeks previously. Her total neostigmine intake on March 1 was 120 mg. of the bromide and 2.5 mg. of the methylsulfate. Weakness persisted until March 3, when the temperature became normal. She again appeared well and strong, and remained so until discharge March 18, 1950. Neostigmine was stopped after the morning tablet on March 12.

Follow-up Observations.—Since discharge the patient has required neostigmine. She was well controlled on 4 tablets of neostigmine bromide daily when last seen on June 20, 1950. On this dose she is able to perform the usual duties of a housewife.

The outstanding features of the case of myasthenia gravis in the mother are the following: (1) the unusual initial symptomatology of the patient had allowed the disease to go undetected for 16 months; (2) the patient experienced a remission during the first five months of pregnancy; (3) a relapse occurred during the sixth month of pregnancy; (4) a remission occurred on the day of delivery; (5) a relapse followed the delivery, and in turn was followed by a remission; (6) the baby was delivered by cesarean section for reasons not related to the myasthenia gravis.

CASE 2.—The infant at birth was normal, with a vigorous cry. Signs of myasthenia were particularly sought for because of previously reported cases. On Feb. 23, twenty-two hours after birth, the baby was observed to have a weak cry and masklike facies. He did not use the facial muscles to any extent when crying. He was generally inactive and nursed poorly, part of the formula being regurgitated through the nose. No improvement occurred during the next two days. Accordingly, on Feb. 25 at 2 p.m. the baby was given 1 mg. neostigmine bromide in water by mouth. Part of the mixture was regurgitated. After 20 min. the baby was again appraised. The cry was more vigorous, and more facial expression was used in crying. He nursed better than during previous feedings. The test was interpreted as being suggestive but not diagnostic. The baby was given 1 mg. of neostigmine bromide by mouth one-half hour before each feeding. While on this regimen, he did well.

On Feb. 26 the neostigmine was discontinued after the 9:45 a.m. dose. The baby did well until 2 a.m. Feb. 27, when marked weakness was noted; the face was again sad and masklike, the sucking power poor, and the cry feeble and expressionless. At 9:30 a.m. the baby was given 2.5 mg. neostigmine bromide in water by mouth. Within 25 min. there was a dramatic change in the facies. The face had a more intelligent appearance. The cry was vigorous and sustained, reaching a higher pitch than had been previously attained. There was an increase in general activity. Feeding was taken easily. The succeeding three feedings were taken well without further neostigmine.

At 11:45 p.m. Feb. 27, 14 hr. after the last dose of neostigmine, the infant was again found to be lethargic, with a weak and shallow cry. The face was apathetic, expressionless, and drooped. Arms and legs moved only occasionally. Vigorous stimulation produced a minimal response. Two milligrams of neostigmine bromide in water was given by mouth. Within 20 min. there had been a progressive increase in activity, which included raising of the eyebrows, increase in the width of the palpebral fissures, and active, continued movement of the arms and legs. The face became expressive and intelligent. The lips were formed, and the cry was decidedly more vigorous. He took 2 fluid ounces (60 cc.) of formula with vigor and even collapsed the nipple. The change provoked by neostigmine was dramatic. A diagnosis of myasthenia gravis was made.

The baby was given 1 mg. of neostigmine bromide in water 15 min. before each feeding. In the days that followed, the facial appearance was strikingly more expressive than before neostigmine was started. On March 3 the neostigmine dosage was reduced to 1 mg. before every other feeding. On March 8, at the age of 15 days, neostigmine was discontinued. The baby remained well. No further weakness had been observed. The baby was well when last seen at age 4 mo.

The outstanding features of the case of myasthenia gravis in the baby are the following: (1) the baby was normal at birth; (2) the symptoms of myasthenia developed gradually from birth so that they were clearly recognized by the second day of life; (3) the diagnosis was easily proved by oral administration of neostigmine bromide; (4) the baby required no neostigmine after 15 days of life.

COMMENT

The course of the mother's disease during her pregnancy does not coincide exactly with any single previously reported case of myasthenia gravis complicated by pregnancy. This is in keeping with the nature of the disease; its course is unpredictable. This is especially true during pregnancy. It is the consensus of other authors that the management of pregnancy and labor in cases of myasthenia gravis should be governed by the same principles as govern nonmyasthenic cases. It was suggested by Adam that purely obstetrical complications would occur from time to time that would demand cesarean section.[2] The case described above presented such complications.

The case of the baby is the seventh case of myasthenia gravis recognized in the neonatal period. The clinical pictures presented by the seven cases are strikingly similar. All seven infants were born of myasthenic mothers. The symptoms were manifest in all by the third day of life. Two of the babies died.[1] The diagnosis was confirmed in five cases by response to neostigmine. One infant was well in five weeks.[1b] In the case presented and one other [3] the patients were well at the end of two weeks. A fourth was well at the end of four months, but still taking neostigmine.[4] The need for continued neostigmine

2. Adam, G. S.: Myasthenia Gravis and Pregnancy, J. Obst. & Gynaec., Brit. Emp. **53**: 557, 1946.
3. Stone, C. T., and Rider, J. A.: Treatment of Myasthenia Gravis, J. A. M. A. **141**: 107 (Sept. 10) 1949.
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in this case was not proved. An infant observed by Ford, cited by Levin,[5a] was well at the end of one week.

Four cases of congenital myasthenia gravis have been described in the literature,[5] the congenital nature being determined in retrospect. The parents of these infants were not myasthenic. These cases seem to fit more closely the classical picture of myasthenia gravis as it is seen in the adult.

Levin suggests that the term "neonatal myasthenia gravis" be used to describe the transient asthenia seen occasionally in newborn babies of myasthenic mothers.[5a] The term "congenital myasthenia gravis" would be reserved for the persistent form of the disease. The distinctive terminology would seem warranted in view of the two distinct clinical courses.

The transient nature of myasthenia in neonatal cases should not cause the clinician to consider the problem lightly. The two deaths reported in this group speak for the seriousness of the disease, in spite of its brief duration.

The cause of myasthenia gravis is unknown. It is known that acetylcholine is an essential agent for the transmission of nerve impulses across the synapses. This agent is normally hydrolyzed by cholinesterase. In myasthenia gravis there exists an excess of cholinesterase with a resulting deficiency of acetylcholine action. Neostigmine acts by temporarily inactivating cholinesterase. The mechanism of the transient myasthenia in the case of the baby described and others is a matter of conjecture. It is certainly related to the mother's illness. It could be postulated that there exists an increase of cholinesterase in the infant. This could be a reflection of an increased circulating cholinesterase in the mother. There is a possibility that an increase in circulating cholinesterase developed in the baby in response to the neostigmine medication administered to the mother. The latter possibility seems more likely, since the baby was well at birth and the symptoms of myasthenia developed in progressive severity several hours after birth. If the increased cholinesterase of the baby were only a reflection of the increased cholinesterase of the mother, it would be expected that the myasthenia would be severest at birth and show progressive improvement. No case of myasthenia gravis in infancy had been observed prior to the introduction of neostigmine (prostigmin®) in 1935.

15880 Green Lawn.

5. (*a*) Levin, P. M.: Congenital Myasthenia Gravis in Siblings, Arch. Neurol. & Psychiat. **62**: 745 (Dec.) 1949. (*b*) Bowman, J. R.: Myasthenia Gravis in Young Children, J. Pediat. **1**: 472, 1948. (*c*) Keynes, G.: The Results of Thymectomy in Myasthenia Gravis, Brit. M. J. **2**: 611, 1949.

Blood Cholesterol in Thyroid Disorders.—Blood cholesterol determinations are of great value in the diagnosis of hypothyroidism, since the range of upward increase in blood cholesterol in hypothyroidism is so wide, up to 800 to 1,000 mg. per 100 cc. Not only is blood cholesterol determination of value in the diagnosis of hypothyroidism, but it is of equal value in checking minus metabolic rates as an indication of the degree of myxedema or hypothyroidism which is present. On the other hand, the downward range of blood cholesterol from normal (160 to 225 mg. per 100 cc.) is of such limited extent in patients with hyperthyroidism that it has little value in corroborating the clinical diagnosis of the latter.—Frank H. Lahey, M.D., Progress in the Diagnosis and Treatment of Hyperthyroidism, *The Surgical Clinics of North America*, June, 1951.

COUNCIL ON PHARMACY AND CHEMISTRY

REPORT OF THE COUNCIL

The Council has authorized publication of the following report.

R. T. STORMONT, M.D., *Secretary.*

PYRIDOXINE HYDROCHLORIDE (VITAMIN B_6)

A STATUS REPORT

Synthesis of vitamin B_6 was accomplished in 1939 [1] and the pure substance available as pyridoxine hydrochloride has been used extensively since that time in clinical trials and in studies of its function in the metabolic processes of animals and bacteria. The vitamin occurs in animal tissues and in other natural source materials, as the compounds pyridoxine, pyridoxal, and pyridoxamine. The term "vitamin B_6" can include any of the three compounds. It has been established [2] that pyridoxal phosphate is the coenzyme for transaminase and tyrosine decarboxylase enzymes that are involved in the interconversion of amino acids and hydroxy acids. Thus the function of vitamin B_6 is related primarily to the metabolism of proteins.

It has been shown that the vitamin is required in the nutrition of all species of animals studied thus far, including the rat, mouse, dog, monkey, chicken, pig, and calf. The vitamin is essential for growth of the young and protracted deficiency results in acrodynia, edema, muscular weakness,[3] and convulsive seizures of an epileptoid type.[4] Microcytic anemia has been observed in dogs [5] fed a pyridoxine-deficient diet, and characteristic neurologic changes in addition to the characteristic anemia have been described in the pig.[6] A recent report [7] describes arteriosclerotic lesions in the monkey after 5½ to 16 months on a pyridoxine-deficient diet. Characteristic excretion of xanthurenic acid, an intermediary metabolite of tryptophane metabolism, indicating a deranged protein metabolism, has been noted by several workers.[8] Although quantitative requirements of animals are not well established, it has been shown that the amount needed by the mouse is dependent to some extent on the protein level of the diet [9] and that the pyridoxine requirements of the rat,[10] dog,[11] mouse,[12] and chick [13] fall in the same general range as those for thiamine.

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In light of the importance of vitamin B_6 in animal nutrition, as demonstrated by these and other reports, clinicians have attempted to discover its importance as a nutrient for man.

Soon after the vitamin became available for parenteral administration, Spies, Bean, and Ashe [14] reported that four undernourished patients exhibiting extreme nervousness, insomnia, irritability, abdominal pain, weakness, and difficulty in walking despite treatment with thiamine, riboflavin and niacin, responded dramatically to administration of vitamin B_6.

A year later Spies, Ladisch, and Bean [15] determined vitamin B_6 excretion after a test dose of 50 mg. in normal males and in ambulatory patients described as B-complex deficient. During the first hour after administration, 8% to 10% of the test dose was excreted by the normal subjects and less than 1% by those diagnosed as having a B-complex deficiency.

These observations of Spies and his group led others to study the effects of this vitamin in a number of clinical conditions. Antopol and Schotland [16] reported improvement in six patients suffering from pseudohypertrophic muscular dystrophy. Changes in such cases are difficult to evaluate, however, and report of improvement was based largely upon subjective findings. Ferrebee and co-workers [17] reported negative results in 20 cases of muscular dystrophy treated with vitamins E and B_6.

Later Rosenbaum, Portis, and Soskin [18] reported relief from extreme muscular weakness associated with neurasthenia one to 14 days following administration of 50 mg. doses of vitamin B_6 in two patients. No response was noted in a patient with myasthenia gravis.

Eaton, Woltman, and Butt [19] concluded from a clinical trial that pyridoxine was of no benefit in amyotrophic lateral sclerosis, progressive muscular atrophy, or progressive muscular dystrophy.

In three separate clinical studies efforts to relieve the symptoms of paralysis agitans with either intravenous or oral administration of pyridoxine resulted in failure. Barker, Stein, Miller, and Wintrobe [20] used intravenous injections of 100 mg. per day over a two-week period in seven patients with obvious manifestations of Parkinsonism. In no case was the slightest evidence of improvement obtained. Zeligs [21] found no beneficial effects whatever in 15 similar patients after repeated injection of 50 to 100 mg. doses of the vitamin. Baker [22] studied 19 cases of paralysis agitans treated with 100 mg. doses of vitamin B_6 by injection, or with daily oral doses of 50 mg. Results of oral medication were suggestive but as a whole the study furnished no basis for concluding that the vitamin is of any value in treatment of this syndrome. Meller [23] studied four cases of postencephalitic and 6 cases of idiopathic paralysis agitans given 50 mg. of B_6 subcutaneously or intramuscularly daily for 10 days, 100 mg. daily for three or four days, and further treatment depending on response for periods of 19 days to five months. As a result he agreed with other investigators that postencephalitic cases fail to respond to B_6 therapy. In the idiopathic form of the disease, decreased pain and rigidity and increased sense of well-being were observed, a result Meller considered significant in a disease of this chronicity.

Results of the use of pyridoxine in dermatology are not conclusive. Wright, Samitz, and Brown [24] reported a two-year therapeutic trial of the vitamin in treatment of various dermatoses. Improvement was noted in several cases of seborrheic or seborrhoid eruptions, but the study did not include control cases and the possibility of spontaneous improvement could not be eliminated. Pyridoxine deficiency, as determined by measure of urine excretion of pyridoxine, was not a reliable index of the patient's response to pyridoxine therapy. Jolliffe, Rosenblum, and Sawhill [25] studied the effect of pyridoxine in treatment of adolescent acne. Although this condition apparently is subject to spontaneous change and seasonal variation, these workers were led to conclude that daily oral doses of 50 to 250 mg. of the vitamin resulted in improvement in the skin lesions. More than 80 patients were observed in the trial.

Following the observation of Chick and co-workers [26] that epileptiform seizures occurred in pigs maintained on a vitamin B_6 deficient ration, Fox and Tullidge [27] studied pyridoxine effects in human epilepsy. Eight boys, 14 to 15 years of age, with varying degrees of petit mal and occasional grand mal seizures, were selected for study because their fits occurred regularly. After treatment with 20 to 100 mg. of pyridoxine daily for four to eight weeks no evidence of increase or decrease of seizures or any other mental or physical change was noted.

In attempts to improve the Army Motion Sickness Preventive which consisted of sodium amytal, atropine, and scopolamine, Smith [28] found that thiamine and pyridoxine alone or in combination were of no demonstrable value.

A number of attempts have been made to determine the value of pyridoxine in preventing or speeding recovery from the nausea and vomiting that occur frequently after large doses of roentgen radiation. As early as 1943 Maxfield, McIlwain, and Robertson [29] reported favorable response in more than 50 patients treated by injection of 25 mg. of pyridoxine at the onset of radiation sickness and then by similar doses daily until relief was obtained. Although enthusiastic about the effect of pyridoxine the authors believed that it should not preclude other medication as needed. In a study of 24 cases Shorvon [30] obtained gratifying results in 22 patients. He observed that oral doses of 50 mg. daily, or two parenteral doses of 50 mg. weekly resulted in comparable responses.

Wells and Popp [31] noted favorable responses when 200 mg. of pyridoxine was injected one-half hour before roentgen treatment. In 200 cases response was excellent or good in two-thirds and fair or poor in one-third. Maximum benefit was noted with injection of 200 mg. but not with 50 mg. or less. The lack of response from placebo treatment was convincing.

Following the early enthusiastic report by Willis and co-workers [32] of the success of pyridoxine in the treatment of 38 cases of nausea and vomiting of pregnancy, Weinstein, Mitchell, and Sustendal [33] obtained similar results. The latter authors

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administered an initial dose of 50 to 100 mg., followed by doses of similar size three times weekly until nausea subsided. Response was most notable in that group of patients in which symptoms were of such severity that hospitalization would ordinarily have been required. These authors concluded that while pyridoxine is of great value, the importance of sedative and diet instructions should not be overlooked. A later report from the same clinic [34] recorded further experience in which the majority of 78 pregnant women treated with pyridoxine responded favorably. The milder attacks of nausea and vomiting were treated with oral doses of 60 to 80 mg. of pyridoxine daily, while the more severe were treated with intravenous doses of 100 mg. daily for a few days, then with daily oral doses of 80 mg. Similar experience has been reported by Silbernagel and Burt.[35]

Failure of pyridoxine in treatment of nausea and vomiting of pregnancy was described by Hesseltine [36] who stated that in his experience hyperemesis gravidarum occurs very infrequently, and that less serious nausea and vomiting, although more common, is difficult to evaluate. From results of a controlled study of 16 cases with varying degrees of nausea and vomiting in which 100 mg. of pyridoxine hypodermically or placebo treatment was given daily, Hesseltine concluded that the use of pyridoxine for hyperemesis gravidarum as advocated in the literature is valueless and without justification.

Clinicians who have reported beneficial results with pyridoxine in treatment of nausea and vomiting of pregnancy have been aware that use of the vitamin was empirical and have been cautious in claiming therapeutic effectiveness. A biochemical basis for such effectiveness has been provided, however, in the recent report by McGanity, McHenry, Van Wyck, and Watt.[37] In an earlier study by this group [38] it was demonstrated by changes in blood urea values that pyridoxine-depleted rats and dogs differed from normal animals in ability to metabolize protein. Following this experiment, blood urea levels were determined in normal non-pregnant women, normal pregnant women, and in 17 pregnant women in the first trimester with nausea and vomiting of a severity classed as hyperemesis gravidarum. The fasting blood urea level was found significantly lower in normal pregnant than non-pregnant subjects. It was even lower in patients with hyperemesis gravidarum than in normal pregnant women, but was restored to normal pregnancy value after the administration of pyridoxine. The response to a test load of an amino acid was studied in the same group of women. Blood urea increased to a maximum six hours after oral administration of 30 mg. of DL-alanine, returning to original values within 12 hours in the non-pregnant and normal pregnant women. In women with hyperemesis gravidarum blood urea levels rose but failed to decrease significantly between the sixth and the twelfth hours, thus exhibiting a flat curve. Supportive therapy alone for 72 hours did not alter response to DL-alanine, but supportive therapy supplemented with 120 mg. of pyridoxine produced normal pregnancy response to the test.

It is difficult to say whether these observations indicate that the biochemical defect in hyperemesis gravidarum is a pyridoxine insufficiency or a defective protein metabolism leading to excessive excretion of amino acids that are effectively deaminated in the presence of additional amounts of pyridoxine.

From the work of Umbreit and Gunsalus [39] it is clear that pyridoxine is transformed in the body to pyridoxal and pyridoxamine, and that pyridoxal phosphate is the co-enzyme for the systems essential for the decarboxylation and transamination reactions in amino acid metabolism. The exact position of the phosphate in the pyridoxal molecule has not been determined.

A number of workers have been concerned with the need for pyridoxine in human nutrition and it appears now to be well established that in man this vitamin has a specific function. Suggestive evidence was furnished by Hawkins and Barsky [40] who observed mild changes in the blood white cell picture in a male subject maintained on a pyridoxine-deficient diet for 56 days. Greenberg and co-workers [41] observed in two human subjects, on a pyridoxine-deficient diet for an extended period, that excretion of xanthurenic acid was greatly increased after a test dose of tryptophane. This xanthurenic acid excretion was reduced following the administration of pyridoxine. The relation of the excretion to xanthurenic acid, a product of tryptophane metabolism, to pyridoxine requirement was first observed by Lepkovsky, Roboz, and Haagen-Smith,[42] who isolated the compound from the urine of rats on a pyridoxine-deficient diet. A recent report from Mueller and Vilter,[43] in which they describe symptoms of pyridoxine deficiency resulting from the ingestion of the pyridoxine analog desoxypyridoxine, further supports the conclusion that there is a human need for this vitamin, as indicated by the following excerpt:

"Eight patients suffering from various chronic illnesses were given 60-150 mg. of desoxypyridoxine intramuscularly daily while they were maintained on a diet low in vitamins of the B complex. Hematologic studies were done before and at biweekly intervals after the institution of the experimental regime. Urine assays for pyridoxic acid, thiamin, riboflavin, and N[1]-methylnicotinamide were done at weekly intervals in most instances. When the deficiency state developed, the patient was placed on a vitamin B complex mixture devoid of pyridoxine and later on pyridoxine alone. The desoxypyridoxine and diet were continued throughout the entire experimental period.

"Seborrhea-like skin lesions developed about the eyes, nose, and mouth within two to three weeks in seven of the eight patients. In three of the seven the lesions were quite severe. Half of the patients developed erosions in and around the mouth resembling cheilosis of riboflavin deficiency and glossitis resembling morphologically that seen in niacin deficiency. One patient developed severe systemic symptoms. A mild but definite lymphocytopenia appeared in seven of the eight patients. No anemia occurred. These manifestations were unchanged when the vitamin B complex mixture devoid of pyridoxine was given but responded in 48 to 72 hours of the parenteral administration of 100 to 200 mg. of pyridoxine."

It is the authors' opinion that the lesions described are specific for pyridoxine deprivation and constitute at least a part of the human syndrome of this deficiency.

A specific demonstration of the need for pyridoxine in human nutrition is found in the report of Snyderman, Carretero, and Holt.[44] Their summary of their results is stated as follows:

"A pyridoxine-deficient diet, given for therapeutic reasons to two mentally defective infants for 76 and 130 days respectively, failed to produce clinical benefit but yielded information of nutritional interest. Both subjects developed evidences of pyridoxine deficiency, indicating that pyridoxine is a human dietary essential. The first change noted was the prompt disappearance of pyridoxic acid from the urine and a reduction of the total urinary pyridoxine to low values ranging from 0.2 to 2 mg. per day. Subsequently, both infants lost the ability to convert tryptophane to nicotinic acid, an effect which was desired in order to block a metabolic path for tryptophane that might be competing with normal tissue synthesis. A plateauing of the weight curve occurred 33 and 73 days after the institution of the regime. On the 76th day one subject developed a series of convulsions which were promptly relieved by the administra-

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tion of pyridoxine. The other subject developed a hypochromic anemia at approximately the 130th day. This responded dramatically to pyridoxine; a rise in reticulocytes was noted after 72 hours reaching a peak in four days after which red cell count and hemoglobin rose to normal. Both subjects gained weight normally after supplementation. In marked contrast to the excellent and prompt clinical response to the administration of pyridoxine was a delay in the reappearance of the ability to convert tryptophane to nicotinic acid."

These last two studies provide evidence that there is a human dietary requirement for pyridoxine.

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

Corticotropin.—Acthar (Armour).—

Actions and Uses.—The adrenocorticotropic hormone of the anterior pituitary gland stimulates the adrenal cortex to secrete its entire spectrum of hormones. Hormonal effect can be exerted only if a functioning adrenal cortex is present. Corticotropin is rapidly utilized in the body; its effect rarely exceeds six hours. This necessitates repeated administration of the drug. The physiologic and metabolic effects of the hormone are due to the adrenal corticosteroids elaborated and are, in general, similar to those described for cortisone acetate. Because of its rapid absorption and utilization these effects appear more promptly than with parenteral or oral administration of cortisone acetate. The prompt fall of the circulating eosinophil count when therapeutic doses of corticotropin are given is the basis for the Thorn test of adrenocortical response. The drug is of value in the same disease conditions for which cortisone acetate is used except that it is not effective for the treatment of Addison's disease.

In general, long term administration of either corticotropin or cortisone acetate induces similar undesired hormonal effects. However, hypertension and virilism are more likely with the use of corticotropin, while cortisone acetate may elicit involution or partial atrophy of the adrenal cortex. A period of depressed adrenocortical function follows sudden cessation of corticotropin administration, but may be avoided by gradual reduction both of the dosage and the number of doses given.

The potent metabolic effects of corticotropin require frequent check on the patient's weight, blood pressure, and electrolyte balance. A high potassium, low sodium intake is advisable if protracted treatment or a large dose of corticotropin is necessary.

Corticotropin is contraindicated for long term treatment in hypertension, diabetes mellitus, mental disturbances, chronic nephritis, congestive heart failure, Cushing's syndrome, and hirsutism. It has been reported that allergic sensitivity to corticotropin may develop in a small percentage of patients; the reactions have varied from anaphylactoid shock to giant urticaria.

Dosage.—The average adult dose of corticotropin is 40 to 50 provisional U. S. P. units daily, administered parenterally in four divided doses. If the desired clinical effect is not obtained, the dosage may be cautiously and gradually increased to a total of 100 provisional U. S. P. units daily. Maintenance dosage should be at the lowest level required to continue clinical improvement.

Tests and Standards.—Corticotropin is assayed biologically by the measurement of the adrenal ascorbic acid response in hypophysectomized rats. An International Standard has been established by the World Health Organization. The provisional U.S.P. unit is identical with the International unit. Each is defined as representing the specific adrenocorticotropic activity of 1 mg. of the International Standard.

Lyophilized Acthar (Pork): Vials containing the equivalent of 10, 15, 25 and 40 provisional U. S. P. units. The Armour Laboratories, Chicago.

Sodium Ascorbate Injection-U.S.P. (See New and Nonofficial Remedies 1951, p. 432).

Solution Sodium Ascorbate: 2 cc. ampuls. A solution containing sodium ascorbate equivalent to 50 mg. of ascorbic acid in each cubic centimeter. Stabilized with 0.1 per cent sodium bisulfite and 0.1 per cent cysteine hydrochloride. Meyer Chemical Company, Detroit.

Solution Sodium Ascorbate: 2 cc. and 5 cc. ampuls. A solution containing sodium ascorbate equivalent to 0.1 gm. of ascorbic acid in each cubic centimeter. Stabilized with 0.1 per cent cysteine hydrochloride. Meyer Chemical Company, Detroit.

Progesterone-U.S.P. (See New and Nonofficial Remedies 1951, p. 361).

Solution Progesterone in Oil with Benzyl Alcohol 2%: 10 cc. vials. A solution in sesame oil containing 25 mg. of progesterone in each cubic centimeter. Preserved with 0.004% phenylmercuric benzoate. Biophysics Laboratories, Inc., Los Angeles.

Solution Progesterone in Oil: 10 cc. vials. A solution in peanut oil containing 10 mg. or 25 mg. of progesterone in each cubic centimeter. Preserved with 0.5 per cent chlorobutanol. Carlo Erba, Inc., New York.

Tetanus Toxoid, Alum Precipitated-U.S.P. (See New and Nonofficial Remedies 1951, p. 383).

Tetanus Toxoid (Alum Precipitated): 5 cc. vials (five immunizations). Preserved with thimerosal 1: 10,000. Pitman-Moore Company, Division of Allied Laboratories, Inc., Indianapolis.

Tetanus Toxoid Alum Precipitated: 2 cc. vials (one immunization) and 10 cc. vials (five immunizations). Preserved with thimerosal 1: 10,000. E. R. Squibb & Sons, New York.

Tyrothricin-U.S.P. (See New and Nonofficial Remedies 1951, p. 44).

Solution Tyrothricin 2%: 50 cc. vials. A 92% alcohol solution containing 20 mg. of tyrothricin in each cubic centimeter. Parke, Davis & Company, Detroit.

Tetanus Toxoid-U.S.P. (See New and Nonofficial Remedies 1951, p. 382).

Tetanus Toxoid Fluid: 1 cc. vials, for supplementary immunizations. Preserved with thimerosal 1: 10,000. E. R. Squibb & Sons, New York.

Amphetamine Sulfate-U.S.P. (See New and Nonofficial Remedies 1951, p. 188).

Powder Amphetamine Sulfate: Bulk; 100 gm. and 1 kg. packages for compounding use. Biorganic Laboratories, Inc., Brooklyn.

Theophylline-Sodium Glycinate (See New and Nonofficial Remedies 1951, p. 304).

Tablets Cinaphyl: 0.16 gm. and 0.33 gm. U. S. Patent 2,433,765. B. F. Ascher & Company, Inc., Kansas City, Mo.

Chloramphenicol-U.S.P. (See New and Nonofficial Remedies 1951, p. 118).

Capsules Chloromycetin: 100 mg. U. S. Patents 2,483,871, 2,483,884, 2,483,886, 2,483,892. Parke, Davis & Company, Detroit.

Hexachlorophene (See New and Nonofficial Remedies 1951, p. 52).

Septisol: 3.78 liter bottles, 18.9 liter pails and 113.5 and 208.1 liter drums. A soap containing 2% hexachlorophene. Vestal, Inc., St. Louis.

Mephenesin (See New and Nonofficial Remedies 1951, p. 165).

Tablets Tolulexin: 0.5 gm. E. S. Miller Laboratories, Inc., Los Angeles.

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ACTH NOMENCLATURE AND STANDARDIZATION

The pituitary adrenocorticotropic hormone (ACTH) was originally given the generic designation of corticotrophin in 1938 by the Third International Conference on the Standardization of Hormones of the League of Nations. Recently this name was reconsidered and again approved by the World Health Organization's Subcommittee on Non-Proprietary Names of the Expert Committee on the International Pharmacopeia. The adoption of the "-trophin" suffix posed a problem because the "-tropin" ending is generally used in the United States to describe activity directed toward stimulating a specific organ. Both suffixes are derived from the Greek: "-trophos" referring to nutrition, "-tropos," to a turn. After considerable deliberation, the Council on Pharmacy and Chemistry has decided to utilize the generic designation of corticotropin for the description of the hormone in New and Nonofficial Remedies. This generic name is not only more consonant with local usage but also more descriptive of the actual hormonal effect which is turned toward the adrenal cortex. This pituitary principle does not provide nutrition for the adrenal cortex.

The variation in nomenclature between the World Health Organization's and the Council on Pharmacy and Chemistry's generic designation for corticotropin is minor and should not cause confusion. In fact, the World Health Organization recognizes that minor differences in spelling may occur because of language variation and national usage.

Of more serious nature, however, has been the problem of standardization of corticotropin. Originally, the dosage of the hormone had been expressed in milligrams, and many physicians undoubtedly believed that the weight statement on the label represented the weight contents of the vial. Since corticotropin is not a pure active principle or chemical entity, but varies in potency with each lot prepared, it had been standardized by comparing the biologic activity of each new batch extracted with an arbitrarily selected house reference standard of corticotropin, utilizing the assay method suggested by Sayers, Sayers, and Woodbury. Label designations of 20 mg. thus did not mean that the vial contained 20 mg. of substance but rather that the content of the vial had the same potency by biologic assay as 20 mg. of the house reference standard. This procedure of standardization is customary for comparing an unknown sample of a biologic principle of variable potency with an arbitrary unit in order to have some uniformity of clinical response.

Subsequently, the World Health Organization's Expert Committee on Biological Standardization adopted the house standard of the original manufacturer as the international standard. The International Unit for corticotropin was defined by the same body as "the specific ACTH activity of one milligram of the International Standard." Although practically the entire supply of this house standard was generously sent to the offices of the World Health Organization, the quantity was extremely limited for world use. The International Reference Standard of corticotropin, necessary for comparative assays and establishment of manufacturers' own reference standards, therefore was furnished in powder form sealed in glass ampuls containing only 1.3 or 4.8 mg. The choice of container was unfortunate, since the powder adhered to the sides of the ampul and could not be entirely shaken free. The amount that could be removed was frequently too small for accurate weighing. The danger of glass particle contamination also existed. Aqueous solutions of the standard could not be utilized because they were unstable and lost potency rapidly. These limitations became evident when several other firms introduced their own brands of corticotropin and found themselves unable to establish a house reference standard in terms of the International Standard. The Food and Drug Administration, therefore, temporarily required each manufacturer to create his own house standard, assay technics, and unit of potency—the objective being for a unit to be comparable in potency with 1 mg. of the first manufacturer's reference standard. No clear interrelationship existed between the variously defined and derived house units. To complicate the matter further, corticotropin derived from the original modified Li method varied in physical characteristics, stability, and yield of hormone from that obtained by the Astwood technic. Nevertheless, each substance produced specific adrenocorticotropic stimulation.

At this juncture, the physician was faced with the unsatisfactory situation of utilizing an inconsistently standardized hormone whose potency varied from brand to brand, as attested by animal experimentation and clinical experience. On March 22, 1951, at the offices of the Food and Drug Administration in Washington, representatives of the firms, of the U. S. P. Committee of Revision, of the Council on Pharmacy and Chemistry, and of the Food and Drug Administration discussed the problem. It was agreed that the most desirable solution would be to set up a provisional U. S. P. reference standard to overcome the shortcomings of the International Reference Standard. Although the U. S. P. Committee of Revision does not usually establish standards for drugs which have not been acted on favorably by the U. S. P. Subcommittee on Scope, in this instance it was felt that the U. S. P. organization could render a distinct service to medicine by creating such a provisional reference standard. It was also agreed that the provisional U. S. P. unit of

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corticotropin should be identical with the International Unit and thus represent the specific biologic activity of 1 mg. of the International Standard for corticotropin.

A supply of corticotropin was obtained from three commercial sources in the United States and pooled and compounded in such a way as to incorporate 0.1 mg. of the powder into a 20 mg. tablet. The office of the U. S. P. Committee of Revision also had obtained a substantial quantity of the International Standard in powder form and similarly compounded this material into tablets weighing about 20 mg. and containing 0.1 mg. or 0.1 International Unit. In comparative assay as measured by the Sayers or the Sayers-Munson method, it was ascertained that the provisional U. S. P. reference standard contained 0.12 International Units per 20 mg. tablet. Further studies on improvement of corticotropin assay are now under way by a U. S. P. study panel.

It now becomes possible and desirable for all manufacturers to label their products in terms of the provisional U. S. P. unit, thus providing some assurance of uniformity among the various brands of corticotropin. Physicians should note that, while corticotropin will then be standardized biologically, the effects in human beings of the various commercial preparations will not be completely comparable, because the assay method does not overcome the known differences between animal and human response. Furthermore, all brands of corticotropin are not made by the same process. Certain differences among brands are evident, such as stability in solution, solubility in saline solutions, and rate of absorption. Clinical experience will have to determine which process of manufacture yields the most desirable product. Then, further measures may be taken to eliminate differences in response by agreement on a uniform method of extraction of corticotropin.

DA COSTA'S SYNDROME, OR NEUROCIRCULATORY ASTHENIA

The appearance in 1940 of the second edition of Sir Thomas Lewis's "The Soldier's Heart and the Effort Syndrome" [1] focused the attention of physicians once more on one of the most frequent causes of invalidism among soldiers. Because the symptoms resembled those of fatigue following effort in normal persons, Lewis suggested the name "effort syndrome." The name "neurocirculatory asthenia" was suggested by a team of medical reserve corps officers of the American Army [2] sent to Colchester, England, to study the condition with Sir Thomas Lewis. They felt that the symptoms comprising effort syndrome in normal persons were not the same as those observed in neurocirculatory asthenia. Da Costa described its occurrence many years ago in the United States. He stressed that the condition was not confined to soldiers, since the symptoms were frequently present before enlistment. Fever, diarrhea, wounds, and strenuous existence of the soldiers were predisposing factors.

The more recent contributions by Wood,[3] by Cohen and his co-workers,[4] and by Walker [5] suggest that the basic mechanism of neurocirculatory asthenia has not been elucidated. The term "effort syndrome" is incorrect, in the opinion of Wood, because the symptoms of the syndrome are not confined to exertion. They may occur at any time during the day or night, and they are invariably provoked by emotion. The tendency is to regard it as a functional disorder of the autonomic nervous system of psychogenic origin. Given a neuropathic predisposition based on hereditary and constitutional inadequacy, many factors can assume the role of exciting or initiating agents. The syndrome is characterized by dyspnea, easy fatigability, palpitation or heart consciousness, fainting, giddiness, headache, sweating, blueness or mottled coloring of the hands, dermatographia, and a variety of neurovascular phenomena. The pulse at rest and at sleep is normal but is easily accelerated by emotion or exercise and is abnormally slow in its return to normal after exercise. Blood pressure is as a rule normal at rest but exhibits the same exaggerated response to exercise and emotion as does the pulse. The electrocardiogram does not reveal any structural changes.

Diagnosis of the syndrome presents few difficulties. The diagnostic problem involves recognition of possible associated disease, such as pulmonary tuberculosis, exophthalmic goiter, malaria, coronary artery disease, thyrotoxicosis, and chronic infections. Wood [3] stresses that patients with Da Costa's syndrome experience a true sensation of breathlessness in circumstances that would not affect a normal person. Hurried, irregular, and shallow breathing is common in the more nervous patients, apart from effort; frequent deep sighs occur in many; in a few there is true hyperventilation, usually the result of emotion.

Emotional reaction is the essential common factor in this syndrome. According to Wood the special feature that distinguishes this group from other psychoneurotic physical patterns is the establishment of a link between the emotional reaction and effort. The link was usually forged when emotional symptoms were misinterpreted and the heart blamed, so that fear of effort followed. Wood concludes that Da Costa's syndrome, as he would prefer to call it, is an emotional reactive pattern peculiar to psychopathic personalities and to subjects with almost any form of psychoneurosis. Walker [5] believes that all the manifestations of the syndrome can be explained as a normal physiologic response to anxiety.

The therapeutic problem is to induce the patient to recognize that he is suffering from the effects of emotional disturbance and not from an organic disease. Psychotherapy must be directed primarily toward recognition and removal of fears and anxiety. In certain instances it may become imperative to alter the environment. Occasional use of barbiturates is useful but is never curative. Prognosis depends much on early recognition and early psychotherapeutic treatment.

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4. Cohen, M. E.; White, P. D., and Johnson, R. E.: Neurocirculatory Asthenia, Anxiety Neurosis or the Effort Syndrome, Arch. Int. Med. **81**: 260 (March) 1948.

5. Walker, W. J.: The Patient with Functional Cardiovascular Disorders (Neurocirculatory Asthenia), Am. Heart J. **42**: 97 (July) 1951.

LOCAL HEALTH UNITS

Evidence is accumulating that the idea of local public health units is receiving favorable attention in an ever-widening circle. This idea is expressed as Point 6 in the 12-point program of the American Medical Association for the advancement of medicine and public health, reading as follows:

> Establishment of local public health units and services and incorporation in health centers and local public health units of such services as communicable disease control, vital statistics, environmental sanitation, control of venereal diseases, maternal and child hygiene and public health laboratory services. Remuneration of health officials commensurate with their responsibility.

A recent release by the National Health Council indicates that a number of states are making substantial progress in the establishment and expansion of local health unit services. The report also points out that legislation now before the House Interstate and Foreign Commerce Committee providing for federal aid to local public health units is in danger of being by-passed unless Congressmen are made aware of its desirability.

Medical service is the core of any local health unit, and the profession, through action of the House of Delegates of the American Medical Association, is formally on record as approving the principle of local health units. But, as physicians have learned, mere approval is usually not sufficient to bring about a desired goal. With the increased attention that is being given this subject, individual practitioners have a double duty to assist in furtherance of the program. Enactment of a federal law facilitating the setting up of local health units will be an important forward step in making available health needs that the profession knows can be provided satisfactorily only at the local level. Unless practicing physicians are closely identified with such programs at all stages, they run the risk of being overlooked when the time comes to decide how a given health unit shall function best at the local level.

HEREDITARY OBESITY

The production of a hereditarily obese strain of mice has been recently reported by Ingalls and associates.[1] Whereas the weights of young adult normal mice are in the range of 16 to 26 gm., the young adult obese mice weigh 38 to 56 gm. A study of the nutritional and metabolic abnormalities of these obese animals is currently reported by Mayer [2] and associates of Harvard University and Jackson Memorial Laboratory, Bar Harbor, Maine.

Ten obese and seven non-obese mice were placed in individual cages and given a free choice of three diets, each diet consisted of a mixture of fat, carbohydrate, and proteins fortified with minerals and vitamins. In one diet 90% of the total calory content was in the form of protein. The second diet contained 90% carbohydrates, the third 90% fats. They found that obese mice ate on an average five calories more per day than the non-obese controls, sufficient to give a 16 gm. increase in body weight by the end of 30 days. The obese mice also selected proportionally more fat and less protein and carbohydrate.

Since the diet selected by the obese animals was suggestive of the restricted carbohydrate diet often prescribed for diabetic patients, quantitative studies of blood sugar were made. It was found that normally fed obese mice had a high blood sugar level, general above 200 mg. per 100 cc. Non-obese controls had a blood sugar level of the order of 110 mg. per 100 cc. After a four-hour fast, the blood sugar level of the obese animals fell 50 to 60%, whereas that of the controls underwent no appreciable change.

The livers of the obese mice were characterized by a glycogen content far below that of the controls. Obese mice also had glycosuria. These observations demonstrate the existence of hereditary diabetes independent of environmental factors. It was further found that obese diabetic mice are insulin-resistant. Even massive doses fatal to normal mice produced no demonstrable toxic symptoms and no fall in blood sugar.

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2. Mayer, J.; Dickie, M. M.; Bates, M. W., and Vitale, J. J.: Free Selection of Nutrients by Hereditarily Obese Mice, Science **113**: 745 (June 29) 1951.

LOS ANGELES BECKONS

Those who are planning to attend this year's Clinical Session of the American Medical Association in December have a bonus awaiting them: a holiday in sunny California, away from winter's slush and snow, and an opportunity to enjoy the scenic beauty and unsurpassed recreational facilities of Los Angeles. The superlatives applied to this city by its Chamber of Commerce are not without foundation. Located in the center of picturesque Los Angeles County, the city is within easy reach of colorful orange groves, snow-capped mountain peaks, and coastal beaches. Served by seven scheduled airlines and three transcontinental railroads, it is readily accessible to visitors from all parts of the country. Its 1,271 hotels have accommodations for every taste and purse, and its numerous specialty restaurants, with their international cuisine, cater to the tastes of the most discriminating gourmet. Entertainment is available in variety and abundance. Los Angeles has been called the talent capital of the country. Hollywood is an integral part of the city, and its movie, radio, and television studios draw thousands of visitors each year, as do the fashionable residential districts and exclusive shopping centers of Beverly Hills. Other attractions in Los Angeles include its beautiful homes and public buildings, its ancient Spanish missions, the old Mexican shops of Olvera Street, the exclusive private mansions of Bel Air Park, Griffith Park and its planetarium, and Chinatown. Among the fine hospitals of interest to visiting physicians is the 2,452-bed Los Angeles County Hospital, one of the largest and best equipped in the country. For the athletically inclined the city boasts year-round golf, tennis, and swimming. For those who have a day or two to spare before or after the Session there will be opportunities to visit one of the many nearby beaches or Santa Catalina Island, with its flying fish and submarine gardens. Here indeed is an opportunity to mix pleasure with business and to profit from both.

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MEDICAL NEWS

ALABAMA

Company Presents Hospital to Communities.—The Lloyd Noland Hospital in Fairfield has been presented by its owner, the Tennessee Coal, Iron and Railroad Company, to the Lloyd Noland Foundation for the benefit primarily of the people of the western sections of Jefferson County. Presentation of the hospital and all of its properties, equipment, and facilities, along with a substantial cash contribution for working funds, was made Aug. 29. An additional sum of $75,000 was donated by the company to erect and equip an outpatient clinic buiding to be operated in conjunction with the 300-bed hospital. The first four members of the board of trustees were selected by the communities, which include Fairfield, Ensley, and Bessemer. The Tennessee Company selected the other three initial trustees of the foundation, the president, treasurer, and comptroller. In the legal instrument establishing the trust, provisions were included whereby the people of the principal western communities will select the succeeding trustees. The Lloyd Noland Hospital includes wards and semiprivate and private accommodations for both white and Negro patients. In addition to clinics for all principal phases of medicine and surgery, it has a modern x-ray department, a fully integrated laboratory, operating rooms, laundry, nurse's home, motor vehicles, and other equipment. Its grounds embrace about 41 acres. The contribution of the hospital by the Tennessee Company to the community and the resultant foundation arrangement will enable the hospital to reach into even greater realms of research, Mr. Wiebel, president of the company, said. He further stated, "It will open up to the hospital means of participating in grants and endowments for medical undertakings heretofore not available to it as a private institution. This should result in further advancement of the entire Birmingham community in the field of medical science."

CALIFORNIA

Dr. Forsham to Direct Laboratory.—Dr. Peter H. Forsham, Boston, has been appointed director of the Research Laboratory in Arthritis and Allied Diseases at the University of California School of Medicine, San Francisco. The arthritis laboratory has been in operation for nearly a year and was established through a legislative grant that called for a joint effort on both the San Francisco and Berkeley campuses. Work to find new materials for use against the diseases is being carried on in Berkeley, while a broad clinical application and research program is going ahead at San Francisco. The laboratory in San Francisco is housed in temporary quarters pending completion of special facilities. Dr. Forsham, has been on the staff of the Harvard Medical School and the associated Peter Bent Brigham Hospital, Boston.

COLORADO

Fall Postgraduate Conferences.—The University of Colorado School of Medicine, Denver, is presenting the following postgraduate courses: (1) Conference on Chest Diseases, Oct. 18-20, co-sponsored by the Colorado Trudeau Society and the American College of Chest Physicians; (2) Heart Disease, Nov. 15-17, co-sponsored by the Colorado Heart Association and the state department of public health, with Drs. Paul D. White, Boston, Gordon B. Myers, Detroit, and John P. Hubbard, Philadelphia, lecturers; (3) Poliomyelitis, Dec. 13-15; (4) Pathological-Physiological Seminars, Tuesday evenings beginning Sept. 24 and continuing through Dec. 15. Inquiries may be made to the Office of Director of Graduate and Postgraduate Medical Education, 4200 E. Ninth Ave., Denver 7.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

DISTRICT OF COLUMBIA

Annual District Meeting.—The Medical Society of the District of Columbia will convene an annual session Oct. 1-3 at the Hotel Statler under the presidency of Dr. Frank D. Costenbader. Visiting speakers include the following:

Richard H. Freyberg, New York, Practical Considerations of the Management of Common Rheumatic Diseases.
Alan C. Woods, Baltimore, The Role of Corticotropin (ACTH) and Cortisone Therapy in Ophthalmology.
John J. McGraw Jr., Bryn Mawr, Pa., Blood Dyscrasias, Their Treatment by Cortisone and by Corticotropin.
Rulon W. Rawson, New York, Use of Corticotropin in Treatment of Neoplastic Diseases.
E. Cowles Andrus, Baltimore, Factors in the Selection of Cases for Surgery on the Heart Valves.
William S. Tillett, New York, Practical Aspects in the Clinical Use of the Streptococcal Enzymes, Streptokinase and Streptodornase.
Everett I. Evans, Richmond, Thermal and Radiation Injury in Atomic Warfare.
James S. Tyhurst, Halifax, Nova Scotia, Panic Syndrome in Atomic Warfare.
Paul H. Holinger, Chicago, Causes and Significance of Hoarseness.
Samuel M. Peck, New York, Fungus Infections and Their Treatment.
Maurice L. Tainter, Rensselaer, N. Y., Rationale of Selection Between Sympathetic Stimulants.
Howard C. Taylor Jr., New York, Carcinoma of the Cervix.
Winslow T. Tompkins, Philadelphia, Nutritional Deficiencies as a Causative Factor in Premature Labor and Toxemia.
Paul C. Swenson, Philadelphia, Evaluation of Roentgen Procedures in Obstetrics.
Meredith F. Campbell, New York, Congenital Obstruction of the Urinary Tract.
Joseph Hiram Kite, Atlanta, Early Diagnosis and Management of Some Problems in Pediatric Orthopedics.
Edmund R. McCluskey, Pittsburgh, Use and Abuse of Sulfonamides and Antibiotics.

There will be sectional round table discussions from 2 to 4 p. m. each day.

FLORIDA

City Gives Hospital Site.—In ceremonies Aug. 28 city officials of Winter Park presented a deed to 18 acres of city-owned property valued at $50,000 to the Memorial Hospital Trust Association. The Memorial Hospital Trust Association of Winter Park was organized in March by a group of citizens who realized the need for a city hospital. The fund drive is expected to open early this fall. Plans for a 40-bed hospital have been drawn, and the ground acquired from the city will allow for building expansion, a nurses' home, and adequate parking areas. The goal for the hospital drive has been set at one million dollars, one half of which will go into the building fund, and one half into a trust fund for maintenance. All funds are expected to be raised locally with no aid from state or federal sources.

ILLINOIS

Health Services for Children.—Three new health services for children have been initiated by the state department of public welfare. They are (1) a hospital specializing in psychiatric treatment for children under 18, to be located in Chicago's Medical Center District; (2) a diagnostic and treatment ward for emotionally disturbed children at Illinois Neuropsychiatric Institute; (3) a unit for the treatment of youthful mental patients at Galesburg Research Hospital.

Public Health News.—Dr. George A. Wiltrakis, Saint Charles, has resigned as deputy director of the Illinois Department of Public Welfare, a position he has held for the last six years. After Sept. 1 he will devote his time to private practice and serve as consulting surgeon to the various institutions of the department. Dr. Wiltrakis has been in the Illinois state medical service since 1930, having been staff surgeon at the Elgin State Hospital, and assistant superintendent of the Alton State Hospital and the Peoria State Hospital. Dr. Walter H. Baer, superintendent of Peoria State Hospital, Peoria, has been appointed acting deputy director succeeding Dr. Wiltrakis.

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Chicago

Personals.—Dr. A. C. Ritchie, pathologist at the University of Oxford for several years, has become a visiting member of the faculty of the Chicago Medical School and will work in the laboratory of cancer research there.——Agnes A. Sharp, Ph.D., chief psychologist and director of research of the Psychiatric Institute of the Municipal Court, was honored at a dinner given by the institute staff Aug. 29. Dr. Sharp, who has been connected with the institute since 1933, will become superintendent of the volunteer program in state hospitals, a two-year study of rehabilitation techniques using volunteers from communities where the hospitals are located. She resigned her position with the institute to accept the state program appointment.

Chicago Medical Society Postgraduate Courses.—Two postgraduate courses are to be presented next month by the society at Thorne Hall, Lake Shore Drive and Superior St. A course in endocrine and metabolic diseases will be given Oct. 15-19, and a course in obstetrics and gynecology, Oct. 22-26. The registration fee for each is $60. The minimum registration is 50 and the maximum 100. Checks should be made out to the Chicago Medical Society and sent to Willard O. Thompson, M.D., Chicago Medical Society, 86 E. Randolph St., Chicago 1. Visiting faculty for each course includes the following:

ENDOCRINE AND METABOLIC DISEASES

Ray F. Farquharson, Toronto, Canada, Functions of the Anterior Lobe of the Pituitary.
E. Perry McCullagh, Cleveland, Diagnosis of Pituitary Tumor.
John R. Mote, Philadelphia, Effect of Corticotropin (ACTH) on the Symptomatology of Disease.
John E. Howard, Baltimore, Clinical Applications of Corticotropin and Cortisone (Allergic Conditions).
Olof H. Pearson, New York, Clinical Applications of Corticotropin and Cortisone (Neoplastic Diseases).
Samuel F. Haines, Rochester, Minn., Functions and Diseases of the Thyroid Gland.
Henry H. Turner, Oklahoma City, Thyroid Disorders of Childhood.
Paul Starr, Los Angeles, Hypothyroidism in Children and Adults.
Edward E. Henderson, Bloomfield, N. J., Osteoporosis: Etiology, Diagnosis and Treatment.
Leo T. Samuels, Ph.D., Salt Lake City, Hormones Secreted by the Adrenal Cortex: Their Physiologic Effects.
William W. Scott, Baltimore, Diagnosis and Treatment of Adrenal Cortical Tumors.
Lawson Wilkins, Baltimore, Diagnosis and Treatment of Adrenal Cortical Hyperplasia.
Dwight J. Ingle, Ph.D., Kalamazoo, Mich., Effect of Cortisone in Health and Disease.
Earl T. Engle, Ph.D., New York, Pituitary Gonadal Interrelations.
Warren O. Nelson, Ph.D., Iowa City, Preparation and Interpretation of the Testicular Biopsy.

OBSTETRICS AND GYNECOLOGY

Earl T. Engle, Ph.D., New York, Physiology of Menstruation and the Hormonal Control of the Menstrual Cycle.
Fred A. Simmons, Boston, Ovulation Timing.
Willard M. Allen, St. Louis, Functional Uterine Bleeding
Charles L. Buxton, New York, Abuses of Hormonal Therapy.
John Rock, Brookline, Mass., Treatment of Menstrual Disorders.
James T. Bradbury, Sc.D., Louisville, Progesterone: Demonstrations of the Induction of Secretory and Decidual Changes in Normal and Castrate Women.
John L. McKelvey, Minneapolis, Toxemias of Pregnancy.
William C. Keettel, Iowa City, Induction of Labor.
Ralph E. Campbell, Madison, Wis., Prolonged Labor and Its Treatment.
Duncan E. Reid, Boston, Heart Disease in Pregnancy.
Carl P. Huber, Indianapolis, X-ray Pelvimetry.
Richard W. Telinde, Baltimore, Carcinoma of the Uterus with Reference to Diagnosis and Treatment.

MISSOURI

Lectures for General Practitioners.—The postgraduate division of the Washington University School of Medicine in conjunction with the St. Louis branch of the American Academy of General Practice will present a series of lectures for general practitioners on Tuesdays and Thursdays from 8 to 10 a. m. in the first floor auditorium of the north building of the medical school. The lecturers are all members of the university medical school staff. Following each lecture there will be a question period. The course started Sept. 18 and will continue through Oct. 25. Information may be obtained from Dr. Ben Eiseman, Assistant Dean, Washington University Medical School, 4580 Scott Avenue, St. Louis 10.

MONTANA

Conference on Physicians and Schools.—The Montana Medical Association will sponsor its second Conference on Physicians and Schools Oct. 5 in the Capitol Building, Helena. The conference will emphasize the development of a school health program in every community, utilizing private medical and dental personnel now available. Fred V. Hein, Ph.D., consultant of the Bureau of Health Education of the American Medical Association, Chicago, will participate in the discussions. This conference will provide an opportunity for all concerned to discuss the problems of a school health program.

NEVADA

State Medical Meeting.—The Nevada State Medical Association held its annual meeting in Reno, Sept. 13-15 under the presidency of Dr. Walter F. Quinn, East Ely. Out-of-state speakers included the following:

John Z. Bowers, Salt Lake City, Medical Problems with Atomic Weapons.
John W. Cline, San Francisco, President, American Medical Association, Common Lesions of the Breast.
Ludwig A. Emge, San Francisco, The Estrogen-Cancer Hypothesis.
Rutherford T. Johnstone, Los Angeles, Occupational Diseases: Diagnostic Problems Confronting the General Practitioner.
Dwight H. Murray, Napa, Calif., What the A. M. A. is Doing for the Doctor.
Wesley E. Peltzer, Salt Lake City, Demonstration-Examination of the Peripheral-Vascular Apparatus, and Diagnostic Consideration of Common Disorders.
Wallace A. Reed, Phoenix, Ariz., Emergencies in Anesthesia.
G. Arnold Stevens, Beverly Hills, Calif., Surgical Treatment of Duodenal Ulcer.

The Woman's Auxiliary met in conjunction with the association.

NORTH CAROLINA

Proctologic Society Meeting.—The Piedmont Proctologic Society held its annual August meeting in Asheville. Dr. C. Ross Deeds of Hendersonville, president, presided. Officers elected for the coming year are Dr. J. Milton Stockman, Knoxville, Tenn., president; Dr. Charles S. Drummond, Winston-Salem, N. C., vice president, and Dr. B. Richard Jackson, Raleigh, secretary-treasurer. During the scientific session, the following papers were presented:

B. Richard Jackson, Raleigh, Incidence of Postoperative Complications in Anorectal Surgery.
William Galvin, Atlanta, Anesthesia in Proctologic Surgery.
Edgar Boling, Atlanta, Reduction of Postoperative Pain After Rectal Surgery.

TENNESSEE

State Postgraduate Program on Internal Medicine.—The Tennessee State Medical Association began its eighth postgraduate medical education program Sept. 3 in Brownsville. Cooperating in the training program are the University of Tennessee College of Medicine in Memphis, Vanderbilt University School of Medicine in Nashville, the Tennessee State Health Department, and the county medical societies of the state. Dr. John Foley Dee of Springfield, Mass., is conducting this program which deals with internal medicine and circulatory diseases. He will lecture in the following towns on the same night each week for 10 weeks: Brownsville, 8 p. m. Monday at Haywood County Hospital; Covington, 7:30 p. m., Tuesday, Tipton County Health Department; Jackson, 7:45 p. m. Wednesday, Jackson Clinic Library; Bolivar, 7:30 p. m. Thursday, Western State Hospital, and Selmer, 7:30 p. m. Friday at Shackleford Funeral Home. The remainder of the state is divided into nine other circuits with five centers to each circuit where the lectures will be repeated. Two years are required to cover all the circuits in the state. The circuit of which Memphis is a part will hold its meetings next fall. Dr. Dee's 10 lectures include talks on cortisone, corticotropin, and new developments in heart disease. The program of the association just ended has been on psychiatry as applied to medicine. Further information may be obtained from the secretary of local county medical societies.

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TEXAS

Greenwood Lecture.—Dr. A. Earl Walker of the Johns Hopkins Hospital, Baltimore, will give the James Greenwood Lecture in Neurosurgery at the University of Texas Medical Branch, Galveston, Oct. 3, on "Surgery of Involuntary Movement."

Postgraduate Conferences.—The Dallas Southern Clinical Society with the cooperation of the Dallas Society of General Surgeons and the faculty of Southwestern Medical School of the University of Texas will hold a conference in general surgery Oct. 8-10, at the Melrose Hotel and Parkland Hospital in Dallas. The guest speaker will be Dr. Champ Lyons, professor and chairman of the department of surgery at the Medical College of Alabama, Birmingham. From Dec. 10 to 12 the society together with the Dallas Internists' Club and the faculty of Southwestern Medical School will present a conference on recent advances in diagnosis and therapy at the Melrose Hotel. The guest speaker will be Dr. S. Howard Armstrong Jr., chairman of the Rush department of medicine and professor of medicine at the University of Illinois College of Medicine, Chicago. The registration fee for each course is $25 payable to the society at 433 Medical Arts Building, Dallas 1.

WASHINGTON

Heart Disease Symposium.—The third annual symposium of the Washington State Heart Association in cooperation with the Washington State Department of Health on "Diagnosis and Therapy of Peripheral-Vascular Disease" and "Surgical Treatment of Mitral Stenosis" will be held Oct. 19-20 in the Medical School Auditorium of the University of Washington, Seattle. The speakers will be two authorities on peripheral-vascular disease: Dr. Travis Winsor of Los Angeles, and Dr. Norman E. Freeman of San Francisco; and two of the pioneers in the recently developed and much discussed field of mitral commissurotomy: Dr. Robert P. Glover and Dr. O. Henry Janton, both of Philadelphia. In addition to their scheduled papers, the speakers will conduct panel sessions and discuss questions from the audience. There will be no registration fee.

WEST VIRGINIA

Symposium on Peptic Ulcer.—This symposium, sponsored by the Kanawha Medical Society, will be held at the Daniel Boone Hotel in Charleston Oct. 3. It will open at 1:30 p. m. and adjourn by 9 p. m. The program will be presented by Drs. Keith S. Grimson, Robert J. Reeves, Ralph W. Rundles, and James P. Hendrix, all of The Duke University School of Medicine, Durham, N. C. There will be a registration fee of $5, including dinner, which will be served at 6:30 p. m. All interested physicians in West Virginia and adjoining states are invited.

WYOMING

State Medical Meeting.—The 48th annual meeting of the Wyoming State Medical Society will be held at Rock Springs Sept. 27-29 under the presidency of Dr. Karl E. Krueger. Guest speakers and their subjects include the following:

J. Earle Estes, Minneapolis, Occlusive Arterial Diseases of the Extremities.
T. Leon Howard, Denver, Infections of the Upper Urinary Tract in Children.
Bascom W. Palmer, Salt Lake City, The Eye and the General Practitioner.
Leland R. Cowan, Salt Lake City, Treatment of Cancer of the Skin.
John L. Gedgoud, Omaha, Fluid Balance.
Walter Freeman, Washington, D. C., Psychosurgery.
John Gramlich, Denver, Art of the Biopsy.
Gordon C. Whiston, Casper, Wyo., Pelvic Fractures.
Henry W. Meyerding, Rochester, Minn., Giant Cell Tumors.
Paul D. Bruns, Denver, Toxemias of Pregnancy.
Francis K. Burnett and Albert R. Pearce, both of Cheyenne, Wyo., Veterans Medical Benefits at His Home Town.
Gordon Meiklejohn, Denver, Infectious Diseases.

Dr. John W. Cline of San Francisco, President of the American Medical Association, will speak on "Public Relations" at the banquet Friday at 8 p. m. at the Old Timers Building. The Sweetwater County Medical Society will sponsor a smörgåsbord Thursday evening to which everyone is invited. A stag smoker will be held at the Elks Club Wednesday evening following the scientific sessions of the International College of Surgeons. The house of delegates will meet Thursday, Friday, and Saturday. The Woman's Auxiliary will hold its annual meeting during the State Medical meeting.

GENERAL

Heart Association Grants.—Sixty new grants-in-aid in the total amount of $311,912 have been made by the American Heart Association for research studies conducted during the 1951-1952 academic year. The latest total research allocation of $478,662 by the national office represents an increase over the $416,386 appropriated the previous year, based on expanded income. Among the largest of the awards made was one to the Marine Biological Laboratory at Woods Hole, Mass., of $10,000 for a study by Dr. Albert Szent-Gyorgyi of molecular mechanisms in the muscle cell as a basis for understanding the nature of muscular contraction, with eventual extension of the study to the heart muscle. Western Reserve University School of Medicine, Cleveland, received an $18,270 grant for a training school for research investigators in the field of heart and blood vessel diseases under Dr. Carl J. Wiggers.

Midwest Medical Librarians Meeting.—Medical, hospital, and pharmaceutical librarians will meet at Abbott Laboratories, North Chicago, Ill., on Oct. 6 for the 1951 session of the Midwest division of the Medical Library Association. States represented will be Michigan, Indiana, Illinois, Wisconsin, and Minnesota. Speakers will be Chicago librarians Marguerite Prime of the American College of Surgeons, H. H. Henkle of the John Crerar Library, Wilma Troxel of the University of Illinois Library of Medical Sciences, and Gertrude Minsk, University of Chicago biomedical libraries; and Edith Dernehl, Marquette University School of Medicine, Milwaukee; Thomas E. Keys, Mayo Clinic, Rochester, Minn.; Louise Lage, assistant librarian of Lilly Research Laboratories, Indianapolis, and Edith Joannes, associate librarian of Abbott Laboratories, North Chicago.

Transcriptions of Radio Series Available.—The Twentieth Century Fund announces that it has made available transcriptions of the entire radio series "The People Act" as a public service to educational institutions and radio stations and to citizen organizations for use in meetings and group discussions. These transcriptions can be obtained on a free loan basis through the Federal Radio Education Committee (FREC) of the United States Office of Education, Washington, D. C. Each program is recorded on one double-face 16 inch, 33⅓ rpm disc and can be played on any play-back machine that will accommodate a 16-inch recording at the required speed. The transcriptions will be sent out together with a teaching and discussion guide which gives the background of the series and the individual programs, suggests related topics for discussion, and provides a bibliography.The original "The People Act" is a series of 13 half-hour programs jointly produced by the "Living" program unit of the National Broadcasting Company and the Twentieth Century Fund. It was broadcast last winter by most of the stations in the NBC network and overseas by the Voice of America. Democracy in action is the theme of the programs.

Crippled Children Society Meeting.—The annual convention of the National Society for Crippled Children and Adults, will be held at the Palmer House, Chicago, Oct. 3-6. There will be instructional seminars on the diagnosis of cerebral palsy in the young child, physical therapy, occupational therapy, speech therapy, social and emotional adjustment, special education, and parent education. Among others the following will conduct the seminars: Dr. Meyer A. Perlstein, secretary, American Academy for Cerebral Palsy, Chicago; Dr. George G. Deaver, medical director, Lenox Hill Hospital Pre-School Cerebral Palsy Center, New York; Miss Edna M. Blumenthal, director of rehabilitation, North Carolina Hospital for Cerebral Palsy, Durham, N. C.; Dr. Edward D. Greenwood, Menninger Foundation, Topeka, Kansas; and Evelyn Millis Duval, Ph.D., executive secretary, National Council on Family Relations, Chicago. Other speakers include Dr. Theodore G. Klump, chairman, Task Force Mobilization, who will lead a panel discussion on the role of the handicapped; Miss Mary Switzer, director, United States Office

of Vocational Rehabilitation, and Mr. Henry Viscardi, who will participate in the panel "The Volunteer Agencies' Role," and Margaret Hickey of the *Ladies' Home Journal*, Philadelphia, who will speak on "The Inner Citadel of our Security."

Mississippi Valley Tuberculosis Society Meetings.—The Mississippi Valley Conference on Tuberculosis and the Mississippi Valley Trudeau Society will hold their annual meetings at the Hotel Sherman, Chicago, Oct. 4-6. The Oct. 4 session will be a joint session of the two organizations. Dr. David T. Smith, Durham, N. C., past president of the National Tuberculosis Association, will be the featured speaker of the morning session. Visual aids, public relations, and statistics will be the subjects of the afternoon public health session. Friday morning the subject of the Trudeau session will be "A Study of Cases Coming to Pulmonary Resection Including Medical, Roentgenological, Surgical, and Pathological Features"; and the afternoon subjects, "Immunization with BCG," "Pathogenesis of Tuberculosis," and "Patient Education Regarding Tuberculosis." A clinical pathological x-ray conference will be held at 8 p. m. Friday. Subjects of the Trudeau society's Saturday morning session are the following: "Management of the Silicotic Patient," "Crushing Injuries of the Chest," "The Rationale of Early Surgical Approach to Osseous Tuberculosis and Its Complications," "Genito-Urinary Tuberculosis," and "The Widening Front in the Treatment of Tuberculosis."

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States in the weeks ended as indicated:

Area	Sept. 8, 1951	Sept. 1, 1951	Sept. 9, 1950
New England States			
Maine	6	4	9
New Hampshire	4	2	3
Vermont	1	..	2
Massachusetts	21	13	33
Rhode Island	3	..	8
Connecticut	20	34	33
Middle Atlantic States			
New York	128	119	253
New Jersey	43	45	49
Pennsylvania	89	54	95
East North Central States			
Ohio	102	74	83
Indiana	22	18	26
Illinois	108	128	110
Michigan	120	98	81
Wisconsin	106	104	56
West North Central States			
Minnesota	45	35	41
Iowa	31	33	47
Missouri	33	64	13
North Dakota	4	5	..
South Dakota	5	14	10
Nebraska	28	37	24
Kansas	84	52	35
South Atlantic States			
Delaware	..	1	2
Maryland	13	16	43
District of Columbia	7	6	10
Virginia	14	19	71
West Virginia	21	19	24
North Carolina	16	21	45
South Carolina	2	7	18
Georgia	43	36	24
Florida	8	9	19
East South Central States			
Kentucky	27	20	51
Tennessee	63	56	38
Alabama	33	24	13
Mississippi	32	31	19
West South Central States			
Arkansas	28	33	12
Louisiana	100	27	17
Oklahoma	44	27	41
Texas	73	70	91
Mountain States			
Montana	6	11	1
Idaho	10	7	7
Wyoming	13	5	1
Colorado	92	90	15
New Mexico	6	9	9
Arizona	22	36	4
Utah	44	39	2
Nevada	..	..	..
Pacific States			
Washington	20	23	59
Oregon	12	19	25
California	117	148	72
Territories and Possessions			
Alaska	1	4	..
Hawaii	1	..	1
United States	1,871	1,746	1,744

American Academy of Pediatrics.—The academy will hold its annual meeting Oct. 22-25 at the Royal York Hotel, Toronto, Canada, under the presidency of Paul W. Beaven, Rochester, N. Y. The meeting will be preceded by seminars Oct. 20-21. General scientific sessions are made up of the following symposiums and panels:

Physiological Consideration of Respiratory Disease, Julius H. Comroe, Philadelphia, chairman; James L. Wilson, Ann Arbor, Mich.; Willis J. Potts, Chicago; James L. Whittenberger, Boston.

The Academy Looks at Pediatric Education, Lee Forrest Hill, Des Moines, Iowa, chairman; Gerald M. Cline, Bloomington, Ill.; Herbert E. Coe, Seattle; Charles F. McKhann, Cleveland; John McK. Mitchell, Philadelphia; Milton J. E. Senn, New Haven, and A. Ashley Weech, Cincinnati.

Neurological Conditions in Children, Francis L. McNaughton, Montreal, Canada, chairman; William A. Hawke, Toronto, Canada; Donald S. McEachern, Donald L. McRae, Wilder G. Penfield, Herbert H. Jasper and James Preston Robb, all of Montreal, Canada.

Carbohydrate Metabolism, Charles H. Best, Toronto, Canada, chairman; Gerald A. Wrenshall, Ph.D., Robert C. Ritchie, Andrew L. Chute, all of Toronto, Canada; Priscilla White and Elliott P. Joslin of Boston, and Alvah L. Newcomb, Winnetka, Ill.

The final symposium will be on Corticotropin, Cortisone, and Allied Substances and Dr. Jerome W. Conn, Ann Arbor, Mich., will be the chairman. Among other speakers will be Professor Arvid Wallgren of the Karolinska Institute, Stockholm, Sweden, who will speak on "Primary Tuberculosis in Childhood"; Professor Stanley Graham, Royal Hospital for Sick Children, Glasgow, Scotland, "Fate of the Primary Tuberculosis Infection in Young Children;" Professor James C. Spence, University of Durham, Newcastle-on-Tyne, England, "Socialized Medicine in England," and Dr. Louis H. Bauer, Hempstead, N. Y., President-elect of the American Medical Association, "Future of Medicine." The banquet will be held Wednesday at 8 p. m. Round table discussions and general sessions will run concurrently.

CANADA

National Immunization Week.—For the ninth consecutive year the Health League of Canada is sponsoring a Canada-wide educational campaign to call to public attention the dangers of such diseases as diphtheria, whooping cough, tetanus, and smallpox, and the means for their prevention. National Immunization Week will be observed Oct. 14-20. Health departments and family doctors throughout the country are able and willing to provide this protection against whooping cough and diphtheria. Dr. Cecil T. Collins-Williams, Toronto, medical director of the Child and Maternal Health Division of the Health League, states that of contagious diseases among children under one year of age, whooping cough is the leading cause of death.

MEETINGS

AMBULATORY FRACTURE ASSOCIATION, Arrowhead Springs Hotel, San Bernardino, Calif., Oct. 8-11. Dr H. W. Wellmerling, 626 Griesheim Bldg., Bloomington, Ill., Secretary.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, Chicago, Oct. 14-18. Dr. W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn., Executive Secretary.

AMERICAN ACADEMY OF PEDIATRICS, Toronto, Canada, Oct. 20-25. Dr. E. H. Christopherson, 636 Church St., Evanston, Ill., Executive Secretary.

AMERICAN ASSOCIATION FOR THE SURGERY OF TRAUMA, The Seigniory, Montebello, Quebec, Canada, Oct. 23-25. Dr. Charles G. Johnston, 1512 St. Antoine St., Detroit 26, Secretary.

AMERICAN ASSOCIATION OF BLOOD BANKS, Hotel Nicollet, Minneapolis, Oct. 22-24. Miss Marjorie Saunders, 3301 Junius St., Dallas 1, Texas, Secretary.

AMERICAN CANCER SOCIETY, New York, Oct. 25. Dr. Charles S. Cameron, 47 Beaver St., New York, Medical Director.

AMERICAN CLINICAL AND CLIMATOLOGICAL ASSOCIATION, Skytop, Pa., Nov. 5-7. Dr. Marshall N. Fulton, 124 Waterman St., Providence, R. I., Secretary.

AMERICAN COLLEGE OF SURGEONS, Fairmont Hotel, San Francisco, Nov. 5-9. Dr. Michael L. Mason, 40 E. Erie St., Chicago 11, Secretary.

AMERICAN HOSPITAL ASSOCIATION, St. Louis, Sept. 17-20. Mr. George Bugbee, 18 E. Division St., Chicago 10, Executive Director.

AMERICAN PUBLIC HEALTH ASSOCIATION, Civic Auditorium, San Francisco, Oct. 29-Nov. 2. Dr. Reginald M. Atwater, 1790 Broadway, New York 19, Executive Secretary.

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AMERICAN ROENTGEN RAY SOCIETY, Washington, D. C., Sept. 25-28. Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Secretary.

AMERICAN SOCIETY FOR THE STUDY OF ARTERIOSCLEROSIS, Chicago, Nov. 4-5. Dr. O. J. Pollak, Quincy City Hospital, Quincy 69, Mass., Secretary.

AMERICAN SOCIETY OF ANESTHESIOLOGISTS, Washington, D. C., Nov. 5-8. Dr. J. Earl Remlinger Jr., 188 W. Randolph St., Room 909, Chicago 1, Secretary.

AMERICAN SOCIETY OF CLINICAL PATHOLOGISTS, Chicago, Oct. 15-20. Dr. Clyde G. Culbertson, 1040 W. Michigan St., Indianapolis 7, Secretary.

AMERICAN SOCIETY OF MAXILLOFACIAL SURGEONS, Drake Hotel, Chicago, Sept. 23-26. Dr. Casper M. Epsteen, 25 E. Washington St., Chicago 2, Secretary.

AMERICAN SOCIETY OF TROPICAL MEDICINE, Congress Hotel, Chicago, Nov. 15-17. Dr. Quentin M. Geiman, 25 Shattuck St., Boston 15, Secretary.

ASSOCIATION OF AMERICAN MEDICAL COLLEGES, French Lick Springs Hotel, French Lick, Ind., Oct. 29-31. Dr. Dean F. Smiley, 185 N. Wabash Ave., Chicago 1, Secretary.

ASSOCIATION OF LIFE INSURANCE MEDICAL DIRECTORS OF AMERICA, New York, Oct. 11-12. Dr. Henry B. Kirkland, P. O. Box 594, Newark 1, N. J., Secretary.

ASSOCIATION OF MILITARY SURGEONS OF THE UNITED STATES, Palmer House, Chicago, Oct. 8-10. Colonel James M. Phalen, Armed Forces Institute of Pathology, Washington 25, D. C., Secretary.

CENTRAL NEUROPSYCHIATRIC ASSOCIATION, Hotel Nicollet, Minneapolis, Oct. 19-20. Dr. Lee M. Eaton, 102 Second Ave. S.W., Rochester, Minn., Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH, Drake Hotel, Chicago, Nov. 2-3. Dr. Kenneth G. Kohlstaedt, 960 Locke St., Indianapolis 7, Secretary.

COLLEGE OF AMERICAN PATHOLOGISTS, Chicago, Oct. 15-16. Dr. Tracy B. Mallory, Massachusetts General Hospital, Boston, Secretary.

DELAWARE, MEDICAL SOCIETY OF, Wilmington, Oct. 8-10. Dr. Andrew H. Gehret, 1007 Park Place, Wilmington, Secretary.

DISTRICT OF COLUMBIA, MEDICAL SOCIETY OF THE, Hotel Statler, Washington, Oct. 1-3. Mr. Theodore Wiprud, 1718 M St. N.W., Washington, Secretary.

GULF COAST CLINICAL SOCIETY, Edgewater Gulf Hotel, Edgewater Park, Miss., Oct. 18-19. Dr. C. D. Taylor, 113 Davis Ave., Pass Christian, Miss., Secretary.

INDIANA STATE MEDICAL ASSOCIATION, Indianapolis, Oct. 29-31. Miss Lucille Kribs, 23 E. Ohio St., Indianapolis 4, Acting Secretary.

INTERSTATE POST GRADUATE MEDICAL ASSOCIATION OF NORTH AMERICA, St. Louis, Oct. 22-26. Dr. Tom B. Throckmorton, Equitable Bldg., Des Moines, Iowa, Secretary.

KANSAS CITY SOUTHWEST CLINICAL SOCIETY, Municipal Auditorium, Kansas City, Mo., Oct. 1-4. Dr. Maxwell G. Berry, 630 Shukert Bldg., Kansas City, Mo., Director of Clinics.

KENTUCKY STATE MEDICAL ASSOCIATION, Columbian Auditorium, Louisville, Oct. 2-5. Dr. Bruce Underwood, 620 S. Third St., Louisville 2, Secretary.

MICHIGAN STATE MEDICAL SOCIETY, Grand Rapids, Sept. 26-28. Dr. L. Fernald Foster, 606 Townsend St., Lansing 15, Secretary.

MIDWEST REGIONAL MEETING AMERICAN COLLEGE OF PHYSICIANS, Columbus, Ohio, Oct. 13. Dr. B. K. Wiseman, Kinsman Hall, Ohio State University, Columbus 10, Ohio, Chairman.

NASHVILLE POSTGRADUATE MEDICAL ASSEMBLY, Maxwell House, Nashville, Tenn., Oct. 3-5. Dr. W. G. Kennon Jr., 647 Doctors Bldg., Nashville 3, Secretary.

NEW HAMPSHIRE MEDICAL SOCIETY, Equinox House, Manchester, Vermont, Sept. 30-Oct. 2. Dr. Deering G. Smith, 44 Chester St., Nashua, Secretary.

NORTH PACIFIC SURGICAL ASSOCIATION, Vancouver, B. C., Canada, Nov. 16-17. Dr. J. A. Duncan, 509 Olive Way, Seattle, Wash., Secretary.

OKLAHOMA CITY CLINICAL SOCIETY, Biltmore Hotel, Oklahoma City, Oct. 29-Nov. 1. Mrs. Muriel R. Waller, 612 Medical Arts Bldg., Oklahoma City, Executive Secretary.

OMAHA MID-WEST CLINICAL SOCIETY, Hotel Paxton, Omaha, Oct. 29-Nov. 2. Dr. L. E. Moon, 1031 Medical Arts Bldg., Omaha 2, Secretary.

OREGON STATE MEDICAL SOCIETY, Masonic Temple, Portland, Oct. 10-13. Dr. Robert F. Miller, 833 S.W. Eleventh Ave., Portland 5, Secretary.

SOUTHERN MEDICAL ASSOCIATION, Dallas, Texas, Nov. 5-8. Mr. C. P. Loranz, 1020 Empire Bldg., Birmingham 3, Ala., Secretary.

SOUTHWESTERN MEDICAL ASSOCIATION, El Paso, Texas, Oct. 18-20. Dr. W. W. Schuessler, 1415 First National Bank Bldg., El Paso, Texas, Secretary.

SOUTHWESTERN SURGICAL CONGRESS, Hotel Jefferson, St. Louis, Sept. 24-26. Dr. C. R. Rountree, 1227 Classen St., Oklahoma City 3, Secretary.

VERMONT STATE MEDICAL SOCIETY, Equinox House, Manchester, Sept. 30-Oct. 2. Dr. James P. Hammond, 542 Main St., Bennington, Secretary.

VIRGINIA, MEDICAL SOCIETY OF, Virginia Beach, Oct. 7-10. Mr. Richard H. Nash, 1105 W. Franklin St., Richmond, Executive Secretary.

WISCONSIN, STATE MEDICAL SOCIETY OF, Hotel Schroeder and Milwaukee Auditorium, Milwaukee, Oct. 1-3. Mr. Charles H. Crownhart, 704 E. Gorham St., Madison 3, Secretary.

WYOMING STATE MEDICAL SOCIETY, Rock Springs, Sept. 27-29. Dr. Glenn W. Koford, 2020 Carey Ave., Cheyenne, Secretary.

INTERNATIONAL

COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, Central Hall, London, England, July 8-13. Dr. J. H. Harley Williams, Tavistock House North, Tavistock Sq., London, W.C.1, England, Secretary General.

EUROPEAN CONGRESS OF HEMATOLOGY, Rome, Italy, Oct. 3-6. Dr. Sven Moeschlin, Mediz Klinak, Zurich, Switzerland, General Secretary.

EUROPEAN CONGRESS ON RHEUMATISM, Barcelona, Spain, Sept. 24-27. Dr. Gunnar Edström, Lund, Sweden, Secretary.

INTER-AMERICAN CONGRESS OF SURGERY, Buenos Aires, Argentina, Oct. 1-6.

INTERNATIONAL ASSOCIATION OF ALLERGISTS, Zurich, Switzerland, Sept. 23-29. Prof. A. S. Grumbach, Hygiene Institut der Universitaet Zurich, Gloriastr. 32, Zurich, Switzerland.

INTERNATIONAL CONGRESS ON MENTAL HEALTH, Mexico City, Mexico, Dec. 11-19. Mrs. Grace E. O'Neill, Division of World Affairs, National Association on Mental Health, 1790 Broadway, New York 19, N. Y.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, London, England, July 14-19. Dr. A. C. Boyle, 45, Lincoln's Inn Fields, London, W.C.2, England, Hon. Secretary.

INTERNATIONAL SOCIETY OF SURGERY, Paris, France, Sept. 24-29. Dr. L. Dejardin, 141, rue Belliard, Brussels, Belgium, Secretary General.

PAN AMERICAN CONGRESS OF OPHTHALMOLOGY, Mexico City, Mexico, Jan. 6-12. Dr. Luis Sanchez Bulnes, Gomez Farias 19, Mexico 4, D.F., Secretary-General.

PAN AMERICAN CONGRESS OF PEDIATRICS, Montevideo, Uruguay, Dec. 5-8. Dr. Maria Luisa Saldien de Rodriguez, Avenida 18 de Julio, 1246, Montevideo, Uruguay, General Secretary.

PAN PACIFIC SURGICAL ASSOCIATION CONGRESS, Honolulu, Hawaii, Nov. 7-19. Dr. Forrest J. Pinkerton, Suite 7, Young Bldg., Honolulu, Hawaii, President.

EXAMINATIONS AND LICENSURE

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* Memphis, Oct. 14-17. Sec., Dr. Curtiss B. Hickcox, 80 Seymour St., Hartford 15, Conn.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Chicago, March 1952. *Oral.* Chicago, May 1952. Final date for filing application is Feb. 1, 1952. Sec., Dr. George M. Lewis, 66 E. 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Various centers, Oct. 15. Final date for filing applications was May 1. *Oral.* The schedule of oral examinations for 1951 has been arranged on a regional basis as follows: New York, Nov. 12-15, covering Maine, Massachusetts, New Hampshire, New York and Vermont. San Francisco, Oct. 22-24, covering Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington and Wyoming. Final date for filing applications was Sept. 1.

Oral examinations in the subspecialties will be held at the same time and place and on the same distribution.

Exec. Sec., Dr. William A. Werrell, 1 W. Main St., Madison 3.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, Oct. 25-26. *Oral* Chicago, May 1952. Final date for filing applications for the May 1952 examination is Jan. 1, 1952. Sec., Dr. W. J. German, 789 Howard Ave., New Haven 4, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written.* Feb. 1, 1952. Final date for filing applications is Nov. 1. *Oral.* Chicago, June 7-13, 1952. Final date for filing application is Feb. 1, 1952. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Twenty-five centers, Feb. 4-5, 1952. *Oral.* Chicago, October 8-13. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Final date for filing applications for the 1952 Part II examinations is Nov. 30, 1951. Sec., Dr. Harold A. Sofield, 122 S. Michigan Ave., Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 8-12. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PEDIATRICS. *Oral.* Buffalo, Oct. 26-28. Ex. Sec., Dr. John McK. Mitchell, 6 Cushman Rd., Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: Denver, Oct. 27-29. Final date for filing of case reports was Aug. 30. Sec., Dr. Bradford Cannon. Office of the Board: 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Written.* San Francisco, October 28. *Oral.* San Francisco, October 29. Sec., Dr. Ernest L. Stebbins, 615 North Wolfe St., Baltimore 5.

AMERICAN BOARD OF PROCTOLOGY: Philadelphia, Nov. 17-18. Sec., Dr. Louis A. Buie, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral* New York, Dec. 17-18. Final date for filing applications was Sept. 1. Act. Sec., Dr. David A. Boyd Jr., 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various centers, Oct. 1951. Final date for filing applications was July 1. *Written.* Various Centers. March 1952. Final date for filing application is Dec. 1, 1951. Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

BOARD OF THORACIC SURGERY: *Oral.* St. Louis, Nov. 2. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

AMERICAN BOARD OF UROLOGY: Chicago, Feb. 9-13, 1952. Final date for filing applications is Sept. 1. Sec., Dr. Harry Culver, 30 Westwood Rd., Minneapolis 16.

DEATHS

Garrey, Walter Eugene, Nashville, Tenn.; born in Reedsville, Wis., April 7, 1874; received his Ph.D. degree from the University of Chicago in 1900, and his medical degree from Rush Medical College, Chicago, 1909; extension instructor in zoology at the University of Chicago from 1894 to 1898 and fellow in physiology from 1898 to 1900; professor of physiology at Cooper Medical College, San Francisco, from 1900 to 1910; associate professor of physiology at Washington University in St. Louis from 1910 to 1916; professor of physiology at Tulane University in New Orleans from 1916 to 1925; became professor of physiology at Vanderbilt University School of Medicine in 1925, and was professor emeritus there from 1944 to the time of his death; lecturer in general physiology, member of the research staff, and member of the board of trustees of the Marine Biological Laboratory at Woods Hole, Mass.; member of the National Board of Medical Examiners from 1922 to 1934; member at large in the medical division and member of the executive committee in the biological division, National Research Council; member, American Association for the Advancement of Science, and the American Society of Biological Chemists, past president of the American Physiological Society and honorary member of the San Francisco Academy of Medicine; vice chairman of the Section on Pathology and Physiology of the American Medical Association in 1935-1936 and chairman in 1937; member of the Council on Physical Medicine and Rehabilitation of the American Medical Association since 1927, having been chairman of the Council's Committee on Scientific Research; published numerous reports on research in various fields of physiology; died June 15, aged 77, of carcinoma of the bladder.

Harper, Cornelius A. ✠ Madison, Wis.; born near Hazel Green, Wis., Feb. 20, 1864; Columbian University Medical Department, Washington, D. C., 1893; appointed to the state board of health in 1901 and made state health officer in 1904; carried forward a program of disease prevention, promoted health legislation and expanded the department; in 1943 resigned as state health officer but was retained as medical specialist in public health; prepared an authoritative history of public health in Wisconsin, being an actual compilation of the minutes of the state board of health since its inception in 1876; member of the House of Delegates of the American Medical Association in 1914; honorary life member of the American Social Hygiene Association and the Conference of State and Provincial Health Authorities of North America, of which he was president in 1908; past president of the Dane County Medical Society, and in 1931 president of the State Medical Society of Wisconsin; served as secretary of the Wisconsin Anti-Tuberculosis Association; in 1930 received the council award of the state medical society for meritorious service and in 1943 a citation for distinguished service; member of the American Public Health Association; awarded the honorary degree of doctor of science from Lawrence College, Appleton, in 1941, and an honorary degree of doctor of laws from the University of Wisconsin in 1945; died June 26, aged 87, of coronary occlusion.

Bagby, Bathurst Browne, Edwardsville, Va.; born in Stevensville, Va., June 3, 1879; George Washington University School of Medicine, Washington, D. C., 1904; member of the American Medical Association; at one time health officer of Henrico and Southampton counties; for many years director of the state bureau of maternal and child health; served as chief health officer and epidemiologist of the city of Richmond on a temporary basis, retiring in June 1941; during World War II served as civil defense director of Northumberland County; past president of the Virginia Public Health Association; died July 6, aged 72, of coronary occlusion.

✠ Indicates Fellow of the American Medical Association.

Abersold, George William ✠ Wheeling, W. Va.; College of Physicians and Surgeons, Baltimore, 1913; fellow of the American College of Surgeons; served during World War I; affiliated with Ohio Valley General Hospital; died July 26, aged 68, of coronary occlusion.

Allen, Granville Stevens ✠ Lawrence, Mass.; Bellevue Hospital Medical College, New York, 1894; served during World War I; for many years on the staff of Lawrence General Hospital; died July 13, aged 84, of coronary thrombosis.

Anderson, Hascal Blount ✠ Watervliet, Mich.; College of Medical Evangelists, Loma Linda and Los Angeles, 1932; served with the Indian Service; on the staffs of St. Joseph, Mich., Hospital and Community Hospital in Watervliet; died in Mercy Hospital, Benton Harbor, July 20, aged 56, of hepatitis and cardiac decompensation.

Barnes, Albert Coombs, Merion Station, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1892; author of many volumes on art; president of the Barnes Foundation; killed July 24, aged 79, in an automobile accident.

Bartlett, Percy, Hanover, N. H.; Dartmouth Medical School, Hanover, 1900; member of the American Medical Association; professor of surgery at his alma mater from 1915 to 1939, when he became professor of surgery emeritus; fellow of the American College of Surgeons; served during World War I; for many years on the staff of the Mary Hitchcock Memorial Hospital, where he died July 6, aged 80, of cerebral hemorrhage due to arteriosclerosis.

Bass, Leopold, Brooklyn; University of Dorpat Faculty of Medicine, Russia, 1894; affiliated with Maimonides Hospital; died July 16, aged 84, of hypertensive heart disease.

Battle, James Fitzgerald ✠ Seattle; University of Georgia School of Medicine, Augusta, 1923; affiliated with Providence, Columbus and Doctors hospitals; died July 26, aged 58, of coronary occlusion.

Becker, Charles Frederick ✠ Camden, N. J.; Jefferson Medical College of Philadelphia, 1915; specialist certified by the American Board of Psychiatry and Neurology; served in France during World War I; on the faculty of his alma mater from 1922 to 1945; on the staff of Cooper Hospital; died in the U. S. Naval Hospital, Philadelphia, July 23, aged 60, of carcinoma of the prostate with bone metastases.

Brown, Wilson C., Newberry, S. C.; Medical College of South Carolina, Charleston, 1888; died July 1, aged 90, of coronary occlusion.

Cawthon, Edly Wilkerson, Plateau, Ala.; University of Alabama School of Medicine, Mobile, 1908; member of the American Medical Association; fellow of the American College of Surgeons; affiliated with City Hospital in Mobile; died June 9, aged 77, of hypertensive cardiovascular disease.

Cogger, Thomas Walter, Anna, Ill.; Loyola University School of Medicine, Chicago, 1919; served during World War I; on the staff of the Anna State Hospital; formerly affiliated with Newberry (Mich.) State Hospital; died in St. John's Hospital, St. Louis, recently, aged 57, of carcinoma of the esophagus.

Dodds, Susan L. Koons, Long Beach, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; formerly a medical missionary in China; died July 6, aged 77, of carcinoma of the breast.

Drake, Daniel Edgar, Newfoundland, N. J.; University of Vermont College of Medicine, Burlington, 1889; member of the American Medical Association; president of the board of health; affiliated with Idylease Sanatorium for many years; died in Franklin (N. J.) Hospital July 19, aged 87, of arteriosclerotic heart disease.

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Heinen, Gustaf Frederick ✠ Toledo, Ohio; Baltimore Medical College, 1902; died in St. Luke's Hospital July 6, aged 79, of Parkinson's disease.

Hipke, William, Marshfield, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1891; member of the American Medical Association; died in Rogers Memorial Sanitarium, Oconomowoc, recently, aged 86, of arteriosclerosis.

Hudson, Leo Arthur, Lancaster, Wis.; University of Wisconsin Medical School, Madison, 1928; member of the American Medical Association; co-owner of the Lancaster General Hospital; died May 26, aged 58, of coronary thrombosis.

Hyde, Harold Valmore, Boston; Harvard Medical School, Boston, 1914; member of the American Medical Association; formerly on the faculty of Tufts College Medical School; fellow of the American College of Surgeons; on the staff of the Boston City Hospital; died June 21, aged 63.

Jones, George Pierce, Memphis, Tenn.; Vanderbilt University School of Medicine, Nashville, 1902; died June 7, aged 73, of cerebral hemorrhage.

Kemble, Earl Wallace, Golden, Colo.; University of Colorado School of Medicine, Denver, 1913; member of the American Medical Association; died June 27, aged 61, of heart block.

Levitch, Isaiah B., New York; Universität Basel Medizinische Fakultät, Switzerland, 1906; member of the American Medical Association; died in Mount Sinai Hospital May 30, aged 70, of acute myocardial infarction.

Morton, John R., San Marcos, Texas (licensed in Texas under the Act of 1907); in 1936 president of the Hays-Blanco Counties Medical Society; died recently, aged 88, of chronic myocarditis.

Planche, L. Stuart ✠ New Rochelle, N. Y.; McGill University Faculty of Medicine, Montreal, Canada, 1921; member of the American Academy of Dermatology and Syphilology; specialist certified by the American Board of Dermatology and Syphilology; served in the British Navy during World War I; affiliated with New Rochelle Hospital; died in St. John's Riverside Hospital in Yonkers, July 12, aged 55, of coronary thrombosis.

Ploucher, William Allen, Upper Montclair, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1896; died recently, aged 78, of carcinoma of the prostate.

Purcell, Edward, Oakland, Calif.; University of Oregon Medical School, Portland, 1911; member of the American Medical Association; formerly city physician; served in France during World War I; affiliated with the Herrick Memorial Hospital, Berkeley, where he died July 7, aged 68, of coronary occlusion.

Pyle, John Sherman, Toledo, Ohio; Bellevue Hospital Medical College, New York, 1886; formerly trustee of the University of Toledo; affiliated with St. Luke's Hospital; died July 7, aged 86, of carcinoma of the prostate.

Richardson, Harold Edward ✠ St. Paul; born in Stevens Point, Wis., Feb. 17, 1895; University of Minnesota Medical School, Minneapolis, 1920; specialist certified by the American Board of Internal Medicine; member of the Central Society for Clinical Research; fellow of the American College of Physicians; on the faculty of his alma mater; affiliated with Gillette State Hospital for Crippled Children, St. Joseph's, St. Luke's, and Ancker hospitals, and the Charles T. Miller Hospital, where he died June 18, aged 56, of coronary occlusion.

Roth, John LeRoy ✠ Conshohocken, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1918; served on the staffs of Montgomery, Norristown State, and Sacred Heart Hospitals in Norristown; died June 21, aged 72, of coronary thrombosis.

Sarjeant, George Evans, Jacksonville, Fla.; Leonard Medical School, Raleigh, N. C., 1911; died June 14, aged 66, of cardiovascular disease and nephritis.

Shuman, Jesse Elmer ✠ Bloomsburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1891; past president of the Columbia County Medical Society; for many years served on the school board; associated with Bloomsburg Hospital; died recently, aged 81, of complications which developed after a fall.

Snipes, James Johnston, Glendale, Calif.; Medical Department of Tulane University of Louisiana, New Orleans, 1903; for many years practiced in Lincoln, Neb.; served during World Wars I and II; member of the Sons of the American Revolution and president of the Nebraska chapter for two years; died June 14, aged 71, of coronary sclerosis.

Sutton, Richard John, Oakley, Idaho; Chicago College of Medicine and Surgery, 1913; member of the American Medical Association; died June 3, aged 66, of heart disease.

Tapley, Thomas Sumner, Tremont, Maine; University of Vermont College of Medicine, Burlington, 1899; died in McKinley June 16, aged 82.

Thayer, Lewis Gilmore, Grants Pass, Ore.; Gross Medical College, Denver, 1900; died in Portland June 25, aged 83, of arteriosclerosis.

Thomas, George Henry, Minneapolis; Harvard Medical School, Boston, 1895; member of the American Medical Association; died June 3, aged 82.

Thompson, Lillian Marcelletto ✠ Chicago; the Hahnemann Medical College and Hospital, Chicago, 1909; died June 14, aged 77, of coronary occlusion.

Trowbridge, Charles Henry, Spokane, Wash.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1894; died in Spokane Sanitarium June 2, aged 91, of arteriosclerosis.

Ursich, Joseph Ansel, Milwaukee; Northwestern University Medical School, Chicago, 1948; served a residency at Milwaukee County Hospital; died June 22, aged 25, of poliomyelitis.

Valentine, Aloysius W., Washington, D. C.; University of Maryland School of Medicine, Baltimore, 1904; member of the American Medical Association; died in Baltimore July 5, aged 76, of arteriosclerotic cardiovascular disease.

Van Zanten, Wesley William ✠ Sheboygan, Wis.; Marquette University School of Medicine, Milwaukee, 1931; for many years county coroner; died June 4, aged 47, of coronary occlusion.

Wallace, James Henry, Youngstown, Ohio; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1908; member of the American Medical Association; died recently, aged 74.

Wasson, Guy Thornton, Bucyrus, Ohio; Eclectic Medical Institute, Cincinnati, 1903; member of the American Medical Association; past president of the Ohio Public Health Association; for many years county health officer; died June 11, aged 72.

Wellman, Harrison M., St. Petersburg, Pa.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1916; member of the American Medical Association; past president of the Clarion County Medical Society; for many years member of St. Petersburg-Richland school board and the Clarion County school board, and was a past president of both organizations; served four terms as county coroner; died in the Western Pennsylvania Hospital, Pittsburgh, June 7, aged 62.

White, John W., Atlanta, Ga.; Atlanta Medical College, 1891; served as a member of the Fulton County Lunacy Commission; died June 28, aged 88, of arteriosclerotic heart disease.

White, Orton Eugene ✠ Angola, N. Y.; University of Buffalo School of Medicine, 1912; specialist certified by the American Board of Otolaryngology; died in Buffalo General Hospital July 18, aged 62, of arteriosclerotic heart disease.

Wolin, Benjamin Maurice ✠ Chicago; Bennett Medical College, Chicago, 1915; served during World War I; died July 7, aged 61, of bronchogenic carcinoma.

Worthman, Edward H., Louisville, Neb.; John A. Creighton Medical College, Omaha, 1900; died May 29, aged 76, of cardiac decompensation and cirrhosis of the liver.

Yates, Charles Everett ✠ Baldwin City, Kan.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; served during World War I; formerly affiliated with the Indian Service; died June 30, aged 78, of carcinoma of the liver.

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GOVERNMENT SERVICES

ARMY

Brigadier General Hays Named Deputy Surgeon General.—Brig. Gen. Silas B. Hays, MC, on Aug. 24 assumed his duties as Deputy Surgeon General of the Army following a brief ceremony in the office of Maj. Gen. George E. Armstrong, the Surgeon General. He succeeds Brig. Gen. Paul I. Robinson, who will take command of Fitzsimons Army Hospital at Denver, Colo.

In his last assignment as Surgeon of the Japan Logistical Command, General Hays was responsible for management of Army hospitals in Japan, the evacuation of all casualties from Korea, and the furnishing of medical supplies and equipment for both Japan and Korea. During World War II General Hays served as chief of medical supply for the European Theater. He was awarded the Legion of Merit with Oak Leaf Cluster, the Croix de Guerre with Palm, and the Order of Santé Publique from France for his work in that country. On his return to the United States, he was appointed chief of the supply division, Office of the Surgeon General, where he remained until his assignment to the Far East Command in May, 1950.

The new Deputy Surgeon General of the Army, Brig. Gen. Silas B. Hays, MC, is congratulated on his appointment by Maj. Gen. George E. Armstrong, Surgeon General.

New Foot Powder to Prevent Cold Injuries.—Army medical research has developed a new foot powder that reduces foot perspiration, offering partial protection against cold injuries to troops living or fighting in cold weather areas, the Department of the Army announced recently. Arctic tests have shown, according to Maj. Gen. George E. Armstrong, Army Surgeon General, that the foot powder reduces sweating by as much as 24%. This development is of major importance to troops in a cold environment because cold injury more frequently involves the feet than any other extremity. Trenchfoot develops in "wet cold," whereas frostbite is associated with "dry cold." Man's feet perspire under almost all conditions, but the secretion of the sweat glands is especially harmful in cold weather because crystallized particles of perspiration act as conductors of cold, thereby diminishing the insulative value of winter footwear. By reducing foot sweating, the new powder will make the winter soldier's heavy socks and boots more effective against cold injury.

The new preparation has a powdered talc base and contains aluminum chloride and potassium alum, the anhidrotic agents, as well as boric acid, salicylic acid and starch. The initial shipment of the powder will be delivered to the Army this fall and will be issued to troops assigned in cold weather areas including those in Korea. The powder will be packaged in seven separate envelopes contained in one heat-sealed cellulose kit. This is a soldier's one-week supply. Troops will be instructed in its use.

Additional research, using a combination of a rubber-barrier sock and the new foot powder, has shown a 60% reduction in perspiration. A new type rubber boot is being developed that will embody the principle of the rubber-barrier sock to eliminate the extra rubber type sock. It will be used in combination with the foot powder. The foot powder alone is intended to be used where the military situation permits a daily change of socks and shoes.

Recovery Rate High In Korea Soldiers.—Back from a Korean inspection trip, Army Surgeon General George Armstrong reports that early first aid is a major factor in the high recovery rate. Only 25 men out of every 1,000 now die of their wounds, in contrast to the World War II rate of 45 in every 1,000.

Work of the litter bearers is complicated by the rugged terrain, Surgeon General Armstrong said. The average trip by litter to an aid station requires one and one-half hours, although during the recent heavy fighting in the mountainous eastern front six hour trips were not unusual, with eight men assigned to each litter.

He said he questioned more than 150 recently wounded men on how soon they received first aid. "Every one," the Surgeon General reported, "said 'right away' and seemed puzzled at the question. The only occasions I was able to learn about when men were unattended for 30 minutes or more were explained by the fact the aid man assigned to the unit was himself killed or wounded."

General Armstrong praised the line officers for the support they are giving the medical department. "Now, when men are supposed to get suppressive drugs or other regular medication, we know they get it," he said. "As an example of the attitude of commanding officers, General Van Fleet has ordered that every electric fan in Korea be used to make patients more comfortable."

Of the wounded, Surgeon General Armstrong said that 26% return to duty without leaving Korea and 61% without leaving Japan. An additional 14% are able to return to duty after hospitalization in the United States. Even a few amputees are sufficiently rehabilitated to return to duty.

Surgeon General Armstrong is hopeful that the new drug primaquine may be found to be a cure for malaria as well as a suppressive. He said recent outbreaks of the disease among Korea veterans is not as serious as it might be because of effective and prompt detection and treatment in this country.

Medical Personnel Win Decorations in Korea.—A preliminary survey reveals that over 2,800 decorations have already been awarded to Army Medical Service personnel for service in the Korean campaign, Maj. Gen. George E. Armstrong, Army Surgeon General, announced Aug. 28. The total includes a posthumous award of the Medal of Honor to Private Richard C. Wilson, aid man with the 187th Airborne Infantry Regiment; 9 Distinguished Service Crosses; 2 Distinguished Service Medals; 149 Silver Stars; 28 Legian of Merit awards; 2 Distinguished Flying Crosses; 11 Soldier's Medals; 1,369 Bronze Star Medals; 9 Air Medals; 126 Commendation Ribbons, and 1,110 Purple Hearts. Eighty-five per cent of the decorations were awarded to Army Medical Service enlisted men. Medical Service Corps officers serving as assitant battalion surgeons, administrators, supply officers, or in similar capacities, received almost 10% of the total. Medical Corps officers received 105 decorations, including 1 Distinguished Service Cross; 2 Distinguished Service Medals; 7 Silver Stars; 18 Legion of Merit awards; 59 Bronze Star medals; 8 Air Medals; 6 Commendation Ribbons, and 4 Purple Hearts.

The tabulation was based on records now on file in the Adjutant General's Office and it is necessarily incomplete since new data arrives periodically from the Far East Command where the decorations are either awarded or authorized.

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Walter Reed Centennial.—Brig. Gen. Sam F. Seeley made the principal address at "Walter Reed Night," celebrated Sept. 1, by the "Faith of our Fathers" pageant, the Sesquicentennial Commission's outdoor presentation in Washington, D. C. The occasion marked the opening of events scheduled to honor the 100th anniversary of the birth of Maj. Walter Reed, famed conqueror of yellow fever, who was born Sept. 13, 1851, at Belroi, Va. General Seeley, MC, is chief of Walter Reed Hospital's surgical service.

NAVY

109th Anniversary for Bureau of Medicine and Surgery.—The 109th anniversary of the Navy's Bureau of Medicine and Surgery was observed on Friday, Aug. 31. The bureau can point to an impressive list of accomplishments since its establishment by an Act of Congress in 1842. Today the Navy operates modern, fully equipped, air conditioned hospital ships in support of sea and land operations. All Navy ships carry a representative of the Medical Department, ranging from an enlisted hospital corpsman, qualified for duty independent of a medical officer, aboard a mine sweeper to the medical officer staffed aircraft carrier with its modern operating room. Ten per cent of the Navy medical officers on active duty have been certified in various specialties by American Boards, and hospital corpsmen are trained in 40 technical specialties allied to medicine. Navy flight nurses are stationed around the world.

Through continuing efforts of the bureau to improve the skill and efficiency of its personnel, new concepts of naval medicine are being developed. Several advances were shown for the first time in Korea: the mobile surgical teams, epidemic disease control units operating with the fleet and in the field with the Marine Corps, and lighter, more compact field equipment. Another facet, the Occupational Health Service Program to promote and conserve the health of the employees of the Navy's industrial establishments, has proven beneficial production-wise.

The Medical Department's record of caring for the sick and injured, its contributions to the art and science of medicine, and the personal sacrifices and valor of its personnel make up an outstanding page in naval history.

Seven years ago while serving as Chief of Surgery at the San Diego Naval Hospital, the present Surgeon General, Rear Adm. Lamont Pugh, observed that, "men as well as ships need a haven for repair." Today, the Navy's Hospital Expansion Program echoes this statement.

Surgeon General Honored by International College of Surgeons.—The Surgeon General of the Navy, Rear Adm. Lamont Pugh, MC, USN, has been selected as an Honorary Fellow of the International College of Surgeons. The diploma and insignia of the college were conferred on him at the 16th Annual Assembly of the United States and Canadian Chapters of the International College of Surgeons, held at the Palmer House, Chicago, Sept. 10-13.

The letter of notification to Admiral Pugh stated, "It was the wish of our Board and our membership that you be so honored because of your many contributions to the art and science of surgery and your constant efforts in advancing the ideals of our great profession."

Send Representative to Industrial Medical Congress.—Capt. Robert W. Babione, MC, USN, director of the preventive medicine division, represented the Navy at the 10th International Congress of Industrial Medicine held Sept. 9-15 at Lisbon, Portugal. The Congress was sponsored by the Permanent Industrial Commission for Industrial Medicine with headquarters at Geneva, Switzerland.

Upon termination of the congress, Captain Babione made a brief visit to the Naval Medical Research Unit at Cairo, Egypt.

First Editor of Armed Forces Medical Journal Retires.—Capt. Joseph L. Schwartz, Medical Corps, USN, formerly of 8203 Grubb Rd., Silver Spring, Md., will be placed on the retired list of the Navy on Sept. 1, after completion of more than 31 years of active military service in the Medical Corps of the Navy. During this time he has held a variety of important posts, including the editorship of the U. S. Armed Forces medical journal to which he was appointed in January, 1950.

AIR FORCE

Human Factors in Flight.—New studies of the airman's reactions to high speed, high altitude, and strange environments are badly needed in the Air Force, Col. Adolph P. Gagge, director of research in the Surgeon General's office, told a group of military and civilian scientists assembled in San Antonio, Texas, Aug. 27-29. The meeting of specialists from universities all over the United States and Canada was held under the joint auspices of the School of Aviation Medicine and the office of the Air Force Surgeon General to plan a research program in the field of psychophysiology.

"During the last years of the war," said Colonel Gagge, "while aircraft development in jets and rockets made tremendous progress, research in the effects produced by these craft on the men who fly them fell far behind, because scientific brains had to be diverted to more immediate problems. For several years after the war, Air Force research was restrained by the policy of strict military economy then in effect. Now we are urgently in need of answers to the questions of human tolerance raised by present-day flight."

Five broad areas of investigation demand research, Colonel Gagge added. These are the following: the care and treatment of flying personnel in modern warfare; results of extreme speed and altitude; conditions found in special environments such as the stratosphere or beyond it, in outer space; flying safety; and the effects of new weapons and unusual methods of warfare. All these, said Colonel Gagge, are fruitful fields of study for psychophysiologists, who deal with the peculiar reactions of the central nervous system to rare and unexpected circumstances encountered in flight.

The conference opened with a welcoming address by Col. Paul A. Campbell, director of research at the School of Aviation Medicine. Presiding was Clifford T. Morgan, Ph.D., chairman of the department of Psychology at Johns Hopkins University in Baltimore. Also present were more than a dozen noted civilian specialists as well as additional representatives of the Surgeon General's office, the School of Aviation Medicine, and the Aero Medical Laboratory at Wright-Patterson AFB in Dayton, Ohio.

School of Aviation Medicine Increases Output.—With the expanding U. S. Air Force impatient for medical officers trained as specialists in aviation medicine, the Air Force School of Aviation Medicine went into high gear and during the past 12 months graduated or enrolled more than 500 Aviation Medical Examiners. In Air Force units, their primary duty will be to conduct physical examinations for flying. On graduation of the current class, which enrolled on Aug. 27, the figure will be well beyond the 500 mark.

Doctors from 72 accredited medical schools in 38 states and the District of Columbia were trained at the School of Aviation Medicine during the scholastic year ending Aug. 31. This was revealed in a recent survey by Dr. Glenn L. Lembke, director of education at the aeromedical school.

In addition, seven foreign nations sent medical officers to the U. S. Air Force school during the same period. These included England, Uruguay, Switzerland, the Philippine Republic, Iran, Egypt, and Nicaragua.

A large majority of the students were reserve officers of the Air Force Medical Corps called to extended active duty due to the nation's rapid military expansion. The regular Air Force, however, and the Air National Guard were well represented in the eight Aviation Medical Examiner classes enrolled between Sept. 1, 1950, and 1951.

New Assignments.—Lt. Col. James W. Humphreys Jr. has been assigned chief of the general surgical section, USAF Hospital, Wright-Patterson Air Force Base, Dayton, Ohio. He came from Fitzsimons Army Hospital, Denver, where he completed three years' residency in surgery. Colonel Humphreys saw action in the European theater as commanding officer of the 430th Medical Battalion and the 30th Medical Group. He was later assigned as staff surgeon to the U. S. Military Mission, Iranian Army, Teheran, Iran. He has received the Iranian award for duty in Iran and the Legion of Merit. He succeeds Lt. Col. Voris F. McFall, who has been assigned as base surgeon at Norton Air Force Base, San Bernadino, Calif.

FOREIGN LETTERS

ITALY

International Scientific Symposium.—An important international scientific symposium, the first since the end of World War II, was held during the past weeks in the Siculorum Gymnasium, which today is the University of Catania. Speakers were W. H. Schopfer (director of the Institute of Botany and Biology of the University of Bern), C. Lian (director of the medical clinic of the Hôpital de la Pitié of Paris), J. Courtois (director of the Institute of Pharmacology of the University of Paris), A. Gigon (director of the medical clinic of the University of Basel), and C. Jiménez-Diaz (director of the medical clinic of the University of Madrid). Among the Italians attending were L. Condorelli (dean of the faculty of medicine of the University of Catania), P. Di Mattei (faculty of medicine of the University of Rome), and G. C. Pupilli (director of the Institute of Human Physiology of the University of Bologna).

ANTAGONISM BETWEEN VITAMINS

It is well known that there are complicated interrelations between the factors of nutrition. Woods demonstrated that the bacteriostatic action of the sulfonamides is due to a mechanism of interference and antagonism among vitamins essential to the bacteria. It was also demonstrated that avitaminosis in man is not always caused by the vitamin that clinically and on laboratory examinations seems to be deficient in the greatest degree. Sometimes an apparent vitamin deficiency conceals antagonistic reactions. For this reason, the administration of large doses of a specific vitamin may produce a paradoxical phenomenon, i. e., a decrease of the natural quantity of that same vitamin (avitaminosis caused by hypervitaminosis).

This phenomenon is difficult to demonstrate in human beings, because of their complicated nutritive equilibrium, but it can be followed step by step in lower organisms as, for example, in Phycomycetes. Prof. Schopfer reported that these micro-organisms require definite amounts of vitamins to grow and to develop. If these amounts exceed a certain limit, the organism becomes vitamin deficient in spite of the excessive amount of vitamin administered. Schopfer demonstrated a disturbance of the vitamin balance by substituting in the culture a vitamin with its antivitamin, by inhibiting the biosynthesis of a vitamin, or by greatly increasing in the culture the percentage of only one vitamin. He thus has clarified two procedures, which he calls "molecular micrurgy" and "molecular teratology." These procedures elucidate the analogous mechanisms observed clinically and therapeutically in man by Waife, Woods, and Fildes.

While the micro-organisms are soon impaired as a result of molecular micrurgy or molecular teratology, the human organism at first defends itself vigorously against the imbalance caused by inadequate doses of vitamins. Therefore, when excessive doses of vitamin are administered, one does not observe the severe damage that, based on the experiment on Phycomycetes, is theoretically expected. The human sets up this "defense" also against the devitaminizing action of some drugs. Dr. Di Mattei proved the existence of devitaminization by examining the urine of many patients to whom he had therapeutically administered special drugs. He found (1) a vitamin that usually is not found in the urine, when the patient was given a certain drug, for example, vitamin A in the urine of syphilitics treated with bismuth compounds; (2) increase in the elimination of specific common vitamins, for example, a great increase in ascorbic acid, which is always present in the urine, following salicylate, barbiturate, or cinchophen therapy, and nicotinamide in the urine of a patient treated with mercury compounds; (3) the disappearance of a common vitamin, for example, disappearance of ascorbic acid following massive doses of quinine or quinacrine hydrochloride (atabrine®), or of nicotinamide following sulfaguanidine therapy.

Thus, drugs can cause avitaminosis by (1) preventing the absorption of nutritive vitamins, as happens when astringents, solvents, or laxatives are administered; (2) stimulating the elimination of vitamins by the urine, as happens when diuretics, cholagogues, and laxatives are administered; (3) speeding up the consumption of vitamins, as when the patient is treated with sulfur, iodine, pyrogenic compounds, or with drugs stimulating metabolism; (4) removing reserves of vitamins from the parenchymal tissues where they accumulate, as may result from treatment with salicylates, barbiturates, or from chemotherapy; (5) preventing the accumulation of vitamins, as by bismuth and by arsphenamine; (6) blocking the endogenous elaboration of vitamins, which happens when one administers intestinal disinfectants (sulfaguanidine or some antibiotics) that are too strong and destroy not only the parasitic intestinal flora but also the flora that produces vitamins; (7) arresting the action of the vitamins, as in the case of administration of sulfonamides, which exert enzymatic antivitaminic activity; (8) preventing the utilization of vitamins, as in cases of ether or chloroform anesthesia.

Another factor causing avitaminosis is encountered after enterocolitis, when one parasitic group of the intestinal flora suppresses the group that forms vitamins. According to Jiménez-Diaz, who lectured on "A New Aspect of Intestinal Autointoxication," sprue, with its many symptoms, is simply an intestinal bacteriosis. Owing to the chronic inflammatory condition of the intestine, the bacteria that destroy the vitamins produced by other bacteria multiply. The patient soon has symptoms of deficiency in vitamins of the water-soluble vitamin B group. Later, other disturbances result from vitamin D deficiency. Then the parathyroid glands, because of calcium lack, elicit the chain of nutritional-hormone disorders that cause either pseudoeclamptic attacks with loss of consciousness or decalcification of important bones, especially intervertebral disks. According to Jiménez-Diaz, sprue can be associated with deficient fat absorption. This, however, is secondary to, or concurrent with, bacteriosis, but is never, as was formerly believed, the predominant cause of the disease. Jiménez-Diaz explains phenomena of histamine overproduction in allergic patients suffering from asthma and chronic recurrent urticaria as correlated with this bacteriosis. The groups of the intestinal flora that produce histamine predominate over the groups that do not produce this substance. Allergic manifestations are caused by the increased production of histamine. Numerous herpetic disorders, notably on the lips and tongue, are the result of destruction by some antibiotics (chloramphenicol) of the intestinal flora that produces vitamin B. Lesions of this type are being cured in France by a combination of antibiotics and of yeasts and ferments rich in vitamin B. It seems likely that the rapid fattening of pigs and of turkeys with broth cultures of antibiotics is due to a selective process of destruction of bacteria that are parasites of the vitamins.

Various interactions of drugs, vitamins, bacteria, and histamine could explain the urticaria produced by sulfonamides. Owing to the action of the sulfonamides, therefore, the histamine-producing flora prevails, which explains the frequent cases of urticaria observed in patients with intestinal disease.

Tumors of the Upper Respiratory Tract.—At a meeting of the Association of Medicine and Natural Sciences of Parma, Prof. Bonati discussed rare neoplasms of the upper respiratory tract. He described a case in which tumors developed simultaneously in two distinct and independent organs. The patient, a man of 53, was a heavy drinker and smoker, syphilitic, and had a pronounced heredity for neoplastic disease from both parents. After one year of severe aphonia, he underwent medical examination. One tumor was observed in the larynx, and a second one, not ulcerated and clearly demarcated from the adjacent tissues, was observed in the posterior part of the right lateral margin of the tongue. Adenopathies suggesting a relationship between the two neoplasms were not observed. Surgical intervention confirmed the observation made on endoscopic examination, i. e., that the tumor was endolaryngeal and was limited to the right vocal cord and the right laryngeal pouch. Microscopic examination revealed the identical structure of the two tumors, which consisted of spinocellular epithelial cells. Some authors tend to exclude from the malignant tumors those of identical structure, while others favor the concept that two or more tumors

The items in these letters are contributed by regular correspondents in the various foreign countries.

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of identical structure may occur simultaneously in two different parts of the organism without any interdependence.

This clinical case is particularly interesting because of (1) the patient's evident heredity for blastomas (six of the nine members in three generations of his family had malignant neoplasms), (2) the rare location of the tumor (in the larynx and on the tongue), and (3) the presence in the patient of the elements most commonly believed to predispose to malignant neoplasm (syphilis and excessive use of tobacco and alcohol). Among the various pathogenic theories of malignant tumors, Prof. Bonati mentioned that of blastomatous diathesis (Hardy, Bazin) and the theories against this (Hansemmann, Roussy, and Lubarcs) and that of embryonal infiltration (Durante, Ribbert, and Vogt). The speaker is inclined to classify this case according to the first pathogenic theory, that of blastomatous diathesis.

At another meeting of the association, Prof. A. Rossi discussed acute tuberculosis of the hilus, recently described by Greppi and Dogliotti. He spoke of its relatively high incidence, emphasized the difficulties of early diagnosis, and discussed the basic importance of the roentgenologic investigation. He reported his own results, based on a study of tracheobronchial adenopathies that he obtained by tomography.

He observed that the shadows of the hilus do not always show the characteristics demonstrated by Greppi and Dogliotti; in fact, the shadow of the hilus, when enlarged and deformed, may have a marmoreal or areolar instead of a homogeneous aspect, with contours sometimes diffuse, sometimes clear and polycyclic. In every case, however, sectional roentgenography shows that, when the median plane is reached, the perihilar shadow, which was observed on direct examination, is in some phases homogenous, while in others it appears as a group of nodular patches surrounded by an opaque halo varying in size. Moreover, it is possible to distinguish clearly the perifocal exudative infiltration in the various layers.

If the lesion is paratracheal, the shadows of the hilus are often associated with perihilar and particularly with mediastinal shadows, which have characteristics identical to those of the shadows of the hilus. These shadows are homogeneous, varying in shape (piriform, quadrangular, or with polycyclic and diffuse contours); they are generally very large, entering the angle of the bifurcation of the trachea in a conelike shape. Sometimes they extend into the entire space between the trachea and the bronchi, either spreading between the primary bronchi or spreading generally into the right side, under the bronchus and the lower lobe. In some cases where the direct examination is negative, sectional roentgenography reveals isolated mediastinal locations. Stenosis of lobar bronchi with atelectasis is frequent. Sometimes the fissures are involved, appearing as capillary or almost capillary striations.

From the observations made in a complete roentgenologic investigation of the thorax, Rossi concludes that the term "acute tuberculous disease of the mediastinum and of the hilus" should be applied to this peculiar clinical picture. The stratigraphic pictures give evidence of a generally postprimary tuberculous form with exudative characteristics. In some cases, however, a late primary form cannot be excluded.

SPAIN

Annual Meeting of Society of Nutrition and Digestion.—The fourth annual meeting of the Spanish Society of Nutrition and Pathology of Digestion was held Dec., 1950, in Madrid, at the headquarters of the Spanish Medical Association (Colegio Oficial de Médicos). Dr. H. G. Mogena presided. The first official topic was diabetes. Drs. J. C. Oya and J. L. Rodríguez-Miñón discussed methods of obtaining experimental diabetes, especially alloxan diabetes. The speakers, in collaboration with Drs. C. Jiménez-Diaz and F. Grande Covián, demonstrated that, even when high doses of alloxan are injected into dogs (100 mg. per kilogram of body weight), it is possible to prevent the onset of diabetes by previously clamping the vascular pedicles of both kidneys. The injection of nondiabetogenic doses of alloxan (30 mg. per kilogram of body weight) to dogs with kidney damage induced by uranium is followed by diabetes. On the other hand, injection of alloxan to depancreatized dogs aggravates the disease considerably. However, if the injection is made after exclusion of the circulation of both kidneys, aggravation of diabetes does not occur. If both kidneys are removed in depancreatized dogs, diabetes becomes worse. Since this effect does not occur in depancreatized dogs when the ureters are ligated, it would appear that aggravation of diabetes following kidney damage or removal is not due to uremic intoxication or deficient urinary elimination of dextrose.

Oya and Rodríguez-Miñón studied alloxan resistance in animals. In dogs that received an injection of alloxan, diabetes developed but disappeared spontaneously, after which the animals became resistant to repeated injections of diabetogenic doses of alloxan, in some cases even 21 months after the first injection. These additional injections did not produce the characteristic initial variations of glycemia or modify the response of the animals to glucose tolerance tests. This response seems to be due to a local immunity in the kidneys and, experimentally, in the liver. The speakers analyzed chronic alloxan diabetes, stressing the differences between this form of experimental diabetes and diabetes due to removal of the pancreas. Two dogs treated with alloxan survived for 1,105 and 1,248 days, respectively. Blood sugar, during fasting, was over 200 mg. per 100 cc., and the animals had severe glycosuria. Insulin was not administered, and ketonuria did not develop.

Histologic study of the pancreas showed lesions of the same type as those described by other observers. However, they are not diffuse as might be expected from diabetes caused by insular lesion only. On the other hand, the same lesions were observed in experimental conditions that were not followed by diabetes, thus indicating participation of the kidneys and the liver in alloxan diabetes.

The second official topic was pathogenesis of diabetes. Dr. L. Castro of the Faculty of Medicine of Seville was the official speaker. He discussed carbohydrate metabolism and its relation to fat and protein metabolism in the genesis of diabetes. He pointed out that the so-called modern period in the study of diabetes started (about 1930) with the publications by Dr. Samuel Soskin (Medical Research Institute of Michael Reese Hospital, Chicago) and collaborators. Castro considers prediabetes a clinical reality, a period during which the metabolism of carbohydrates gradually changes. He also discussed pituitary and thyroid diabetes (Houssay) and recent studies on the relation of sulfur and sulfur-bearing compounds to carbohydrate metabolism. He observed, during experiments, that prevention of the inflow from the vena porta into the pancreas, followed by injection of insulin into the vena porta, results in an increase of blood glutathione content. He discussed the metabolic disturbances involved in the development of diabetes. Dr. Castro agreed in principle with the concept of impaired utilization of dextrose.

The third official topic was treatment of the complications of diabetes. Dr. F. Jiménez García of Madrid was the official speaker. Over a period of 25 years, he treated 2,800 diabetic patients, 83 of whom were in coma. The speaker listed conditions that occur frequently in association with diabetes, such as diseases of the skin, the sense organs, the nervous system, the kidney, the digestive tract, and the cardiovascular system, as well as acute and chronic infectious diseases, trauma, surgery, pregnancy, childbirth, and lactation. He dealt also with insulin resistance, severe acidosis, precoma, hypoglycemic coma, and simple hypoglycemia. He stressed the importance of Root's method of treating coma and of avoiding administration of dextrose solution. He emphasized the need of early control of ketosis and the importance of treating complications, especially coma, in special clinics. The physician should be at the patient's bedside during coma until the patient recovers consciousness. He denied the value of therapeutic rules concerning dosage of insulin in coma. However, he gave approximate rules, stressing that they are not applicable in all cases. He pointed out the frequency of hypopotassemia in diabetic coma and the methods of diagnosis and treatment.

The fourth official topic was diabetes as a social problem. Prof. J. L. Rodriguez Candela of the University of Valladolid was the official speaker. Dr. Hagedorn of Copenhagen lectured on initial stages and early diagnosis of diabetes, Drs. Civeira, Vilaclara, Vidal Ribas, Rocha, Calvo Melendro, Grande, Roda, Oliver Pascual, Castro Fariñas, and Romero Calatayud also read articles on diabetes.

The Spanish Society of Pathology of Digestion and Nutrition has published the papers read at this meeting.

CORRESPONDENCE

APPREHENSION OF MEDICAL EMPLOYEE

To the Editor:—We wish to enlist your aid in apprehending Johanna A. Simendinger, with many aliases. She is described as 25 years, 5 ft. 7 in., 108 lb., born in Johnstown, Pa., on Oct. 25, 1925. Her fingerprint classification is 29/17 W/U 110/110 18/17.

While employed in a local doctor's office, this subject cashed approximately $1,000 worth of checks, forging the doctor's name. Because of her experience in a medical office, she may attempt to seek employment with other physicians.

The accompanying photograph of her was taken in Minneapolis in 1949. If it would be possible to print this photograph in your publication, we feel that it would not only assist us in serving our Forgery Warrant (No. F-3310, Bail $3,000) but would also serve to protect your subscribers. Should this subject be recognized and apprehended, please refer to Long Beach Police Department Crime Report No. 325-910.

WILLIAM H. DOVEY,
Chief of Police, Long Beach, Calif.

PHYSICIANS FOR GUAM

To the Editor:—During the past few years, the Territory of Guam has expanded at a rapid rate. Economically the territory is progressing toward stability, after several years of war and enemy occupation, and this has naturally brought about an increase in commercial activity with a concomitant rise in population.

Prior to the inauguration of civil government for the territory, the naval establishment provided dental care for the civilian population, but now the services of the Navy dentists and technicians are no longer available to the local residents.

Exclusive of the military, there are approximately 30,000 local residents of Guamanian ancestry, and about 3,500 off-island residents. In addition, there are some 7,000 contractors' employees of United States citizenship and some 12,000 contractors' employees of Philippine citizenship. The contractors' employees are cared for on a contract basis.

At the present time there are two private practicing doctors of medicine on the island, and there is a definite need for more.

The Government of Guam maintains a 315 bed hospital with a competent staff, including specialists in most fields of medicine. The hospital has a ward available for private patients and is open for doctors to care for their private patients.

The climate on Guam is very similar to that of Florida or Honolulu. The island is in a most interesting period of political and economic growth and approaching maturity. While rehabilitation is not complete, living can be pleasant and interesting for a person with intelligence, curiosity, and adaptability.

The Government of Guam would appreciate applications from practicing doctors of medicine for a license to practice on Guam. The requirements for obtaining a license on Guam are graduation from a recognized medical school, a license to practice medicine in one of the 48 states or a territory having laws of reciprocity with one of the states, or the taking of an examination in lieu of reciprocity. Any person interested in practicing medicine on Guam should communicate with the Executive Secretary, Commission on Medical Licensure, Government of Guam.

CARLTON SKINNER,
Governor of Guam.

PHOSPHORUS POISONING

To the Editor:—We read your stimulating editorial on "Acute Phosphorus Poisoning" in THE JOURNAL, June 2, 1951 (page 478), with great interest. In bringing the subject of phosphorus poisoning to the attention of the medical profession, there is one practical point which we have encountered (*Gastroenterology* **17**:279 [Feb.] 1951) and feel should be emphasized. This is the latent period or so-called period of quiescence. It is a variable interval of time during which there is a subsidence of symptoms between the original gastrointestinal symptoms and the appearance of systemic complaints. The former symptoms are thought to be due to direct irritation of the gut by the phosphorus, while the later complaints are attributed to the building up of high concentrations of phosphorus in the vital organs. This period of remission may lull the physician into a false sense of security so that he discharges the patient as fully recovered, only to have him return in a day or two with more serious systemic symptoms. Valuable time has been lost, during which vigorous systemic treatment (high carbohydrate diet, intravenous glucose, amino acids, plasma, vitamins, oxygen inhalation and liver extract) should have been employed, thus avoiding tissue damage, shock and often death.

Since, in many cases of phosphorus poisoning, the latent period presents a deceptive picture to the physician of the subsidence of signs and symptoms without apparent recovery, and since an awareness of this latent period may lower the mortality rate because of the continuation of therapy during this crucial time interval, we feel that it should be emphasized in any discussion of acute phosphorus poisoning.

LAWRENCE WECHSLER, M.D.,
RICHARD L. WECHSLER, M.D.,
Montefiore Hospital, Pittsburgh.

ADIE'S SYNDROME

To the Editor:—Your correspondent Dr. Wartenberg (THE JOURNAL, July 21, 1951, page 1152) appears to have overlooked the fact that the association of a tonic pupil and the absence of tendon reflexes was first described in England by Markus in 1906. The reference is C. Markus, Trans. Ophthalm. Soc. U. K., 1906, *26*, 50. The evidence that Markus first drew attention to the combination of signs often referred to as Adie's syndrome appears to be indisputable.

G. E. BEAUMONT, M.D., F.R.C.P.,
The Middlesex Hospital,
London, England.

NURSING IN SWEDEN

To the Editor:—Some time ago I wrote objecting to your reports on the poor Swedish nursing situation. I regret to report now that university and state hospital nursing is "fair," while private hospital nursing is on a very low level. Sweden is in my opinion headed for state medicine.

ALGOT ÅSTRÖM, M.D.,
c/o A. B. Svenska Hanelsbanken, Stockholm.

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BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Contracts: Failure to Perform Contract for Medical Services.—The plaintiff physicians filed suit against the defendant on an account stated for fees for medical services. From a judgment in favor of the plaintiffs, the defendant appealed to the court of appeals of Georgia, division number 2.

The defendant admitted a promise to pay the amount for which suit was brought but alleged that the plaintiffs' failure to perform their obligations under a contract resulted in damage to the defendant in more than the balance of the amount due, for which reason the defendant should be relieved from liability. The defendant's answer set up that the terms of the contract were that the plaintiffs agreed to give the defendant's wife prenatal care, attend the birth of the child, deliver the child, and give both mother and child post-natal care for six weeks following the birth of the child; that they agreed to use the "twilight-sleep method," the same being the use of certain drugs to render the mother unconscious of pain, such drugs to be administered when labor pains began to occur at three-minute intervals; that the doctor on duty when the defendant's wife entered the hospital would take charge and deliver the child.

The defendant testified that his wife entered the hospital at 4:30 a. m. on December 21 and that Dr. Grimes was on duty at that time. Dr. Grimes told the defendant that when birth pains occurred at three-minute intervals his wife would be given paraldehyde and would thereafter suffer no further pain. At 10:00 a. m. Dr. Grimes left the hospital and Dr. Fish came on duty. He remained until 1:15 p. m. At approximately 2:00 p. m. the defendant's wife began suffering pains at three-minute intervals, but the defendant could not find any of the clinic doctors in the hospital. At about 3:50 he called at the clinic and was informed by Dr. Grimes that Dr. Colvin was supposed to come on duty and that he, Grimes, could not take over Colvin's case. To this the defendant replied that he had contracted for four doctors and not with any one of them and he said he would try to get someone to come over; then Dr. Bartholomew arrived at 4:20 and defendant met him in the hall and urged him to come to his wife's bedside; that he did so; that drugs were thereafter administered; that the child was born at 5:38 p. m.; that the defendant's wife remained under the care of the clinic during the five-day period she was in the hospital, but that afterwards, due to the altercation, the defendant engaged another doctor for the post-natal treatment.

From the defendant's own testimony, said the court, it appears that the agreement contemplated generally that the expectant mother would receive adequate care and the pain relieving drugs, and it would seem that whether the care and drugs she actually received under the circumstances were adequate would be a matter for expert testimony, of which there was none. It does appear, the court continued, that the defendant's wife suffered labor pains at three-minute intervals between 2:00 p. m. and 4:20 p. m., during which time no doctor was in attendance and no pain relieving drugs administered. The damage alleged to have resulted from this was the pain and suffering of the wife during that period. Without entering into a discussion as to whether this would be a proper subject matter for an action to which the husband only is a party, it does appear that there was no guarantee that all or any given amount of pain would be relieved or that all pain would be relieved during any particular period.

It is apparent from its terms that the agreement constituted an entire contract for a given price, the treatment to extend from the time of the agreement until six weeks after birth. So far as the testimony shows, this agreement was fulfilled by the plaintiffs, in so far as they were allowed to do so, for all of this period except 2½ hours on the afternoon of the child's birth. It is true that the defendant's wife received only five days of the agreed six weeks post-natal treatment but this was due to the defendant's action in removing his wife and child from the care of the clinic when they left the hospital. The contract was entire and was not severable. The defendant contended that this being so, the plaintiffs cannot recover unless they have performed all of the obligations imposed upon them under the terms of the contract, and that they did not perform all of these terms in that for the 2½-hour period in question at a time when his wife most needed the services of the doctors, she did not receive them. Granting, said the court, that the failure of the doctors to appear during the time in question constituted a breach of the agreement and that the defendant at that time could have refused all further services from them, procured another physician, and treated the contract as being at an end, he did not do so, but accepted the plaintiff's services at 4:20 that afternoon, through the delivery of the child, and for five days thereafter, not releasing them until after the mother had left the hospital. While it is easily understandable that the defendant would not wish to employ a new physician on the very day his wife was in labor, nevertheless his conduct in retaining them throughout her subsequent stay in the hospital, and in having them proceed with a minor operation on the infant, constituted a waiver of his right to rely upon such breach for the purpose of rescinding the entire contract.

No question was raised as to the reasonableness of the fee for which the plaintiff was suing and the judgment of the trial court in favor of the plaintiff physicians was therefor affirmed.—*Cartwright v. Bartholomew, 64 S.E. (2d) 323 (Georgia, 1951).*

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MEDICAL MOTION PICTURES

Operation Blood Bank: 16 mm., color, sound, showing time 14 min. Produced in 1951 for Cutter Laboratories by Moss Film Productions, San Francisco. Procurable on loan from Cutter Laboratories, Fourth and Parker, Berkeley 10, Calif., or local district offices of Cutter Laboratories.

Blood transfusions have become one of the most frequently employed operative procedures in modern medicine in peace and in war; the development of the technic of storing blood in what has become known as blood banks has made this possible. The need for whole blood is always acute, and the urgency becomes still greater in war and when atomic warfare threatens. Blood is the only product used in medicine that cannot be manufactured and must be obtained from man. All this makes it necessary to spread the information about blood banks and their operation; this is what the film intends to do.

After a brief introduction dealing with the donor procurement activities, the audience is taken behind the scenes of a blood bank. One follows the donor from the moment he enters, has a physical examination, signs a release, and has his blood examined. The audience sees the technic of venipuncture, the handling of the donor, and the collection of the blood, including the extra specimens for additional laboratory tests. After the blood is drawn, the donor is given some refreshment; his blood is placed in the refrigerator and is then shipped from the central blood bank to branch depositories in hospitals.

The various technics employed during the entire process are presented clearly and in sufficient detail to make the film a valuable educational experience for blood bank technicians, nurses, interns, laboratory technicians in general, medical students, and physicians. This film can be used to advantage for the education of lay audiences in order to interest them in blood donations. It will dispel fears among lay persons and make them more amenable to respond to requests for blood. This picture is well organized, and the photography and narration are excellent.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Internal Medicine, Chicago

88:1-134 (July) 1951

*Hormonal Neurogenic Vasopressor Mechanism. R. D. Taylor, I. H. Page and A. C. Corcoran.—p. 1.
Cation Exchange Resin in Treatment of Nephrotic Syndrome. R. W. Lippman.—p. 9.
Blood Volume in Pulmonary Tuberculosis. N. I. Berlin, D. F. Rowles, G. M. Hyde and others.—p. 17.
Potassium Deficiency in Chronic Renal Disease. H. K. Schoch.—p. 20.
*Human Adrenal Cortex After Administration of ACTH and Cortisone: Morphologic Changes. W. M. O'Donnell, S. S. Fajans and J. G. Weinbaum.—p. 28.
Peritoneoscopic Cholangiography. P. G. Keil and S. N. Landis.—p. 36.
Late Effects of Thorium Dioxide in Man. C. Cassel, J. M. Ruffin, R. J. Reeves and L. D. Stoddard.—p. 42.
Hypertensive and Nonhypertensive Periarteritis Nodosa. S. L. Wilens and J. Glynn.—p. 51.
Rational Basis for Use of Low Sodium, High Protein Diet Therapy in Laennec's Cirrhosis. R. M. Kark, R. W. Keeton, N. O. Calloway. —p. 61.
*Epilepsy in Systemic Lupus Erythematosus: Effect of Cortisone and ACTH. P. W. Russell, J. R. Haserick and E. M. Zucker.—p. 78.
Recent Advances in Nutrition: Review of Literature, 1949-1950. G. A. Goldsmith and J. Gibbens.—p. 93.

Hormonal Neurogenic Vasopressor Mechanism.—Taylor and associates have previously reported two observations indicating central nervous system participation in hypertension: first, the hypertensive diencephalic syndrome and, second, a pressor substance in the cerebral ventricular fluid of patients with hypertensive disease. In addition, while cerebral ischemia produces a transitory and unstable hypertension in dogs, a chronic, relatively stable form of neurogenic hypertension can be elicited by adding to the effects of cerebral ischemia prolonged stimulation of the floor of the fourth ventricle. Recently both cerebral baroreceptors, which alter arterial pressure in response to changes in intracranial spinal fluid pressure, and cerebral vessel chemoreceptors, which respond homeostatically to a variety of vasoactive drugs, have been described. The present communication draws attention to the existence of still another central nervous mechanism that acts on arterial pressure. The authors describe cross circulation experiments in dogs with spinal cord pithed below the sixth cervical segment and both vagi cut in the neck. On centripetal vagus stimulation, a vasopressor substance, distinct from epinephrine, arterenol (nor-epinephrine), renin, angiotonin and pitressin was liberated into the blood stream. Its activity was enhanced by large doses of tetraethylammonium chloride and inhibited and ultimately abolished by *l*-hydrazinophthalazine (C-5968). This drug also inhibits the pressor action of serotonin, the pressor and vasoconstrictor substance formed during the clotting of blood. On appropriate stimulation, the brain can act as an endocrine organ that releases a pressor substance into the blood. The hypotensive properties of the phthalazine derivative (C-5968) are consistent with this hypothesis.

Morphology of Adrenal Cortex After Administration of ACTH and Cortisone.—The adrenals of nine patients treated with corticotrophin (ACTH) and of five treated with cortisone were studied. In patients who had received corticotrophin, there was loss of lipids, hypertrophy of the zona fasciculata and zona reticularis, and, in some cases, cortical hyperplasia. The zona glomerulosa appeared narrowed and ill-defined, but some of its cells were hypertrophic. This layer may have responded to the hormonal stimulation by a more rapid transformation of its cells to the fascicular type as a means of augmenting the secretory complex. The described morphologic pattern is believed to be similar to that observed in patients who have been subjected to stress. The adrenal glands of patients who had received cortisone showed atrophy of the fascicular and reticular layers and broadening of the zona glomerulosa. Although the sudanophilic material was reduced in concentration, some was still present as intracellular globules. These changes can be compared to those seen in the adrenal glands following destruction of the pituitary gland. This suggests that cortisone administration induces adrenal atrophy by suppressing the secretion of corticotrophin.

Epilepsy in Lupus Erythematosus.—This study was prompted by the observation of grand mal epileptic attacks in lupus patients with positive L. E. test reactions. The authors of this paper believe that any patient with epilepsy and rheumatoid arthritis may have systemic lupus erythematosus. A review of the literature reveals that among 144 patients with the lupus erythematosus syndrome, there were 22 (15%) who had convulsions. Seven of 28 patients with positive plasma L. E. reactions who have been observed at the Cleveland Clinic since February, 1942, had convulsions. The incidence of this symptom is thus significantly greater in the series of positive L. E. tests than among cases observed prior to the introduction of the plasma L. E. test. Two patients had convulsions for years prior to the appearance of recognizable symptoms of lupus erythematosus. This suggests that epilepsy, when accompanied with rheumatoid arthritis or leukopenia, may constitute a prodromal symptom of systemic lupus erythematosus. Routine electroencephalograms were made on the last 11 patients of the series, abnormal patterns being noted in seven. Electroencephalograms frequently revealed an organic type of dysrhythmia in patients with or without convulsions in systemic lupus erythematosus. Progressive and regressive changes in the electroencephalogram were found to parallel relapses or remissions in this disease. Routine pathological studies in four patients failed to reveal specific brain alterations in lupus erythematosus. Treatment with cortisone and corticotrophin produced improvement in epileptiform seizures related to lupus erythematosus.

A.M.A. Arch. Pathology, Chicago

52:1-104 (July) 1951

Experimental Medullary Necrosis of Kidney: Morphologic and Functional Study. E. E. Mandel and H. Popper.—p. 1.
Problems of Classification of Poliomyelitis Virus. C. W. Jungeblut. —p. 18.
*Coexistent Gastroduodenal and Cerebral Lesions in Infancy and Childhood. H. G. Schlumberger.—p. 43.
Observations on Cytoplasmic Hepatic-Cell Pigment in Man. J. Post, J. G. Benton and R. Breakstone.—p. 67.
Method for Histopathologic Study of Atrioventricular Node, Bundle and Branches. M. Lev, J. Widran and E. E. Erickson.—p. 73.
Granulomatous Glomerulonephritis Associated with Polyarthritis: Report of Case. J. F. A. McManus and A. T. Hornsby.—p. 84.
Portal Axis Thrombosis with Spontaneous Portacaval Shunt and Resultant Cor Pulmonale. F. A. Mantz Jr. and E. Craige.—p. 91.
Note on Origin of Multinucleated Giant Cells from Vascular Channels in Tumors: Tumors Arising in Thyroid Gland, Bone, and Soft Tissue. L. J. Rather.—p. 98.

Coexistent Gastroduodenal and Cerebral Lesions.—In a series of 251 consecutive autopsies on infants and children Schlumberger observed one case of multiple acute gastric ulcers, two cases of gastromalacia, and seven of acute duodenal ulcer; in all these cases the gastric lesion was associated with cerebral damage. Tuberculous meningoencephalitis was found in three of these patients, bulbar poliomyelitis in two, edema and anoxia in two, and intraventricular hemorrhage, sinus thrombosis, and microcephaly in one each. The author suggests that the causal relationships between cerebral lesions and acute gastroduodenal ulcers are multiple and complex. The integrating factors may be nervous or humoral, and perhaps oftenest both. The neural mechanism is probably that suggested by Cushing, i. e., stimu-

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An asterisk (*) before a title indicates that the article is abstracted.

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lation of a parasympathetic center in the diencephalon that secondarily activates cranioautonomic nuclei, especially the dorsal nucleus of the vagus. The resultant autonomic imbalance produces local ischemia or hyperemia with stasis and increased capillary permeability. Either of these vascular changes leads to anoxia and tissue damage with decreased resistance to the action of the gastric juice. The hypothalamus also influences the motility of the gastrointestinal tract and the quantity and the quality of the digestive juices. Increase in gastric hydrochloric acid or pepsin and/or a decrease in the neutralizing bile or pancreatic juice may be important in the production of gastroduodenal ulcers. In conjunction with the well-known neural mechanism, the more recently recognized humoral responses probably play a part. These patients had been subjected to subacute or chronic stress that may have led to the liberation of large amounts of corticotrophin and corticoid hormones, which may have led in turn to increased gastric secretion and to impaired healing of the erosions initially produced by focal vascular changes.

American Journal of Clinical Pathology, Baltimore

21:399-500 (May) 1951

Rh Sensitization Following Repeated Transfusions of Rh-Positive Blood into Rh-Negative Recipients. S. J. Klein, B. E. Konwaler and W. K. Mahany.—p. 399.
Experimental Acute Metastatic Calcification in Kidney of Rats. H. J. Dick and J. T. Prior.—p. 409.
Laboratory Procedures for Rheumatoid Arthritis: Critical Survey of Tests Used in Diagnosis and Treatment. B. B. Wells, R. D. Lowrey and S. W. Ross.—p. 423.
Significance of Fat in Sputum. W. F. Nuessle.—p. 430.
Lymphocytic Response of Diabetic Patients to Administration of Glucose and Insulin. S. S. Lazarus, B. W. Volk, M. Jacobi and others.—p. 436.

American Journal of Ophthalmology, Chicago

34:811-944 (June) 1951

Atomic-Bomb Radiation Cataract: Case Report with Histopathologic Study. S. J. Kimura and H. Ikui.—p. 811.
Esotropia: Incidence, Etiology, and Results of Therapy. R. G. Scobee.—p. 817.
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American Journal of Surgery, New York

81:595-704 (June) 1951

Parenteral Bacitracin in Surgical Infections. A. B. Longacre and R. Waters.—p. 599.
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Primary Carcinoma of Female Urethra with Metastases. J. S. Eisenstaedt.—p. 612.
Carcinoma of Cecum. J. F. Patterson Jr. and J. M. Deaver.—p. 618.
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*Infrequency of Pelvic Endometriosis in Negro Women. G. Blinick and V. J. Merendino.—p. 635.
Surital Sodium: New Intravenous Anesthetic Agent. P. C. Lund.—p. 637.
Use of Kirschner Wire: Forgotten Accessory in Treatment of Intracapsular Fractures of Femur. M. Behrend.—p. 642.

Rarity of Pelvic Endometriosis in Negro Women.—The incidence of pelvic endometriosis was only 0.1% on the gynecologic service at Harlem Hospital, where nearly all patients are Negro women. Uterine adenomyosis was commoner but was found in only 1.14% of laparotomies. The causes of endometriosis are not known, but two facts may help to explain the rarity of endometriosis in Negro women. First, endometriosis is rare in conjunction with pelvic inflammatory disease. This has been repeatedly demonstrated by Sampson and others and is a strong argument to support his theory of pathogenesis by tubal reflux. At Harlem Hospital a large percentage of patients who undergo laparotomy have severe endosalpingitis with tubal occlusion. Second, it has been pointed out that the incidence of pelvic endometriosis is low in ward patients as compared with private patients. This is attributed to earlier marriage and childbearing in the ward patients and this factor probably applies also to the Negro women. A constitutional racial factor may also be involved.

Am. Practitioner & Digest of Treatment, Philadelphia

2:481-568 (June) 1951

Infections of Hand, Diagnosis and Treatment. W. R. Schaffarzick.—p. 481.
Pneumococcal Meningitis: Review of 40 Cases. W. H. Simpson and H. L. Holley.—p. 486.
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Laboratory Aids in Diagnosis of Tuberculosis. M. M. Cummings.—p. 502.
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Blood, New York

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*Studies on Cross Circulation in Man: I. Methods and Clinical Changes. H. R. Bierman, R. L. Byron Jr., K. H. Kelly and others.—p. 487.
Effects of Triethylene Melamine and Related Compounds on Leukocytes of Mouse Leukemia. J. H. Burchenal, L. F. Webber, J. L. Biedler and others.—p. 504.
Effect of Massive Doses of Cortisone on Peripheral Blood and Bone Marrow of the Mouse. H. Quittner, N. Wald, L. N. Sussman and W. Antopol.—p. 513.
*Studies in the Rh Sensitization: I. Methods. II. Effect of Rh-Negative Pregnancies on Rh Antibody Titer. A. S. Wiener, R. Nappi and E. B. Gordon.—p. 522.
Relation of Methemoglobin to Hemolysis. B. B. Clark and R. W. Morrissey.—p. 532.
Deficiency of Plasma Prothrombin Conversion Accelerators in Postoperative State with Description of Simple Method of Assay. R. Warren and J. S. Belko.—p. 544.
Inhibition by Rutin of Capillary Injury by Alpha-Radiation in Rats. J. Q. Griffith Jr. and J. F. Couch.—p. 552.
Certain Hemolytic Mechanisms in Hemolytic Anemia. E. Ponder.—p. 559.

Cross Circulation in Leukemia.—The elevated leucocyte count in leukemia may be due to increased production of white blood cells in the hematopoietic tissues or decreased removal of white cells from the circulating blood by the capillaries of the lung. Leukemic leucocytes infused intravenously into nonleukemic subjects are promptly and almost completely removed from the circulating blood by the lungs of the recipient. To study this phenomenon more fully the authors performed cross-transfusions between leukemic and nonleukemic patients. They describe the methods used for vein-to-vein, artery-to-artery, and artery-to-vein transfusions and conclude that the interarterial method is most satisfactory for investigation of the pulmonary leucocyte removal mechanism. In one child with lymphogenous leukemia there was a pronounced decrease in the leucocyte count after each of three cross transfusions, and a moribund state was succeeded by a transient remission of one month's duration after the first transfusion. In another patient with lymphogenous leukemia an impairment in the pulmonary removal mechan-

ism was demonstrated by the finding of numerous myeloid cells in the arterial blood after an intravenous transfusion of myelogenous blood. An excessive leucocyte removal mechanism was demonstrated in a patient with subleukemic lymphogenous leukemia. Equalization of the number of circulating leucocytes in a leukemic and a nonleukemic patient was not achieved even after a 26-hour cross transfusion, during which 150 liters of blood were exchanged. There was no evidence even at autopsy of the transmission of leukemia to the nonleukemic patients, most of whom had incurable malignant lesions.

Rh-Negative Child and Rh Antibody Titer.—The Rh antibody titer was studied during pregnancy and after delivery in 11 cases in which previously sensitized Rh-negative mothers had Rh-negative babies. In addition, one case was studied in which a type Rh_1 mother, previously sensitized to the rh″ factor, gave birth to a type Rh_1 baby. In all cases the babies were normal at birth and the baby's serum contained univalent Rh antibodies equal in titer to those present in the maternal serum. In no case was there a rise in the antibody titer in the maternal serum either during the pregnancy or after the baby was born. Thus, it has not been possible to confirm claims concerning a "nonspecific anamnestic rise" in Rh antibody titer, said to be caused by an Rh-negative baby. In one of two cases described in detail, there was no appreciable change in Rh antibody titer during the pregnancy, despite the use of so-called Rh hapten, nor had there been an appreciable change in titer for as long as two and one-half years previously. The Rh antibody titer of the baby's blood dropped about 98% by the end of the sixth month, while during the same period of time the maternal antibody titer fell only approximately 35%. From the course of the Rh antibody titer of the baby's serum, the half-life of the antibody globulin molecule is estimated to be about 30 days.

Bulletin New York Academy of Medicine, New York

27:339-404 (June) 1951

Carcinoma of Pancreas and Carcinoma of Ampulla of Vater: Re-Evaluation. W. B. Parsons.—p. 339.
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Cancer, New York

4:441-658 (May) 1951

Neck Dissection. H. Martin, B. Del Valle, H. Ehrlich and W. G. Cahan. —p. 441.
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Familial Distribution of Breast Cancer in a Utah Kindred. C. M. Woolf and E. J. Gardner.—p. 515.
Carcinoma of Sweat Glands. A. P. Stout and S. G. E. Cooley.—p. 521.
Tracer Studies of Radioactive Sodium Estrone Sulfate (S^{35}) in Cases of Advanced Breast Cancer. E. F. Lewison, J. E. Levi, G. S. Jones and others.—p. 537.
Effects of Folic Acid Antagonists and 2,6-Diaminopurine on Neoplastic Disease: With Special Reference to Acute Leukemia. J. H. Burchenal, D. A. Karnofsky, E. M. Kingsley-Pillers and others.—p. 549.
Blood Histamine in Myelogenous Leukemia. M. B. Shimkin, H. R. Bierman, B. V. A. Low-Beer and others.—p. 570.
Histochemical Demonstration of Latent Active Carbonyl Groups in Normal and Neoplastic Nervous Tissue. A. M. Seligman and R. Ashbel. —p. 579.
Mucoid Carcinoma of Rectum. H. D. Trimpi and H. E. Bacon.—p. 597.
*Role of Vertebral Venous System in Metastasis of Cancer to Spinal Column: Experiments with Tumor-Cell Suspensions in Rats and Rabbits. D. R. Coman and R. P. deLong.—p. 610.
Studies on Mechanism of Action of Chemotherapeutic Agents in Cancer: V. Influence of Citrovorum Factor and Folic Acid on Toxic Manifestations of Aminopterin in Mice. E. M. Greenspan, A. Goldin and E. B. Schoenbach.—p. 619.
"Vertical" Transmission of Mouse Mammary Carcinoma and Chicken Leukemia: Its Possible Implications for Human Pathology. L. Gross. —p. 626.
Effect of Radioactive Colloidal Metallic Gold in Treatment of "Acute" AK-4 Leukemia in Mice. P. F. Hahn, H. E. Skipper, E. L. Carothers and L. J. Bernard.—p. 634.

Vertebral Venous System and Metastases to Spinal Column.—Experiments were designed to determine whether embolic tumor cells introduced into the femoral vein could pass directly to the lumbar vertebrae by way of the vertebral veins, by-passing the lungs. If such were found to be the case, then, as suggested by Batson, the spontaneous metastases of pelvic tumors to the lumbar spine in man might be accounted for without the assumption that the embolic cells pass through the capillaries of the lung to be distributed by the arterial circulation. Tumor-cell suspensions were injected into the femoral veins of rats and rabbits while slight abdominal pressure was applied. At autopsy, tumor foci were found in the vertebral venous system of 12 out of 14 rats and of four out of seven rabbits. Most of these tumor foci were found in the lumbar vertebrae, but one each was found in the spinal cord, the venae vasorum of the femoral vessels, and the choroid plexus of the brain. No foci were found in arterioles, where one would expect them to appear if the cells had entered the arterial circulation by traversing the pulmonary blood channels. Cells injected without accompanying abdominal compression resulted, with only one exception, in the appearance of tumors in the lungs only, again indicating failure of the cells to pass through the lung capillaries. These observations are in accord with the concept that the frequency of spontaneous tumor metastases to the vertebral column from pelvic tumors in man depends on the entrance of tumor-cell emboli directly into the vertebral venous system, by-passing the lungs.

Circulation, New York

3:801-960 (June) 1951

Influence of Respiratory Gas Mixtures on Arterial Pressure and Vascular Reactivity in "Normal" and Hypertensive Dogs. I. H. Page and F. Olmsted.—p. 801.
Effect of Priscoline on Peripheral Blood Flow in Normal Subjects and Patients with Peripheral Vascular Disorders. T. B. Van Itallie and C. W. Clarke Jr.—p. 820.
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*Plasma Cholesterol Levels During Rapid Weight Reduction. W. J. Walker and J. A. Wier.—p. 864.
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Pressure Curves from Right Auricle and Right Ventricle in Chronic Constrictive Pericarditis. A. T. Hansen, P. Eskildsen and H. Götzsche. —p. 881.
Advanced Disturbances of Cardiac Mechanism in Potassium Intoxication in Man. H. D. Levine, J. P. Merrill and W. Somerville.—p. 889.
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Unipolar Bronchial Electrocardiographic Exploration of Heart in Man: Preliminary Report. I. Goldstein, L. Pordy, K. Chesky and others. —p. 911.
On Evaluating Einthoven Triangle Theory. J. S. Butterworth and J. J. Thorpe.—p. 923.
Clinical Aspects of Mercurial Diuretics. C. T. Ray and G. E. Burch. —p. 926.

Ammonium Chloride Acidosis.—The occurrence of acidosis is reported in six patients following the administration of 6 to 8 gm. of enteric-coated ammonium chloride daily for seven to 45 days. The acidosis was severe in four patients and nearly fatal in two. Five patients had congestive heart failure and various types of intrinsic renal disease. The remaining patient had subacute glomerulonephritis and anasarca. Clinical manifestations ranged from anorexia, nausea and vomiting with lassitude, to marked stupor, areflexia, and Kussmaul respiration. In all patients rapid improvement followed omission of ammonium chloride and intravenous administration of fluids and lactate. No close relationship between the degree of congestive heart failure, the amount of drug administered, or the severity of acidosis was noted. In three of the patients with congestive heart failure pronounced azotemia developed. The severe acidosis is believed to be related to intrinsic renal disease and the inability of the kidneys to prevent continued loss through the urine of fixed base with chloride. The elevated plasma chloride concentrations observed in ammonium chloride acidosis

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are related to continued intake of chloride, increased tubular reabsorption of chlorides, and, in part, dehydration resulting from pronounced water loss. Decrease in urea clearance and a rise in nonprotein nitrogen were considered as further effects of acidosis in four patients. Two patients had severe anemia, which is known to be associated with decreased renal blood flow, but sufficient data are lacking to assess the role of the anemia in the production of acidosis. Ammonium chloride is a valuable adjunct in the management of congestive heart failure but should be used with great caution when renal disease is suspected or present. It is suggested that the administration of ammonium chloride be limited to three consecutive days per week. When longer periods of administration are necessary, careful observation of the patient and measurement of the blood carbon dioxide combining power are indicated.

Plasma Cholesterol Levels During Rapid Weight Reduction.—Twenty-seven obese patients were placed on reducing diets of 600 or 800 calories daily after their weights had been recorded and the fasting plasma cholesterol level had been ascertained. Forty plasma cholesterol determinations were made during the period of rapid weight reduction; 27 were lower, and 30 higher than earlier control levels. There seemed to be no significant increase or decrease in cholesterol levels during the first two weeks of weight reduction. Determinations taken during the third week averaged 32.5 mg. per 100 cc. lower than control values. Patients undergoing most rapid weight loss showed the greatest drop in plasma cholesterol. The diet offered to the patients was extremely low in fat and relatively high in protein and bulk. Many fears concerning rapid weight reduction have been based on the concept that weight reduction would cause increased fat mobilization, with consequent elevation of blood cholesterol, since it is one of the chief vehicles for fat transport. Results in these patients indicated that fear of elevating the plasma cholesterol need not deter the physician from subjecting obese patients to rapid weight reduction.

Delaware State Medical Journal, Wilmington

23:105-136 (May) 1951

Present Status of Antibiotic Therapy. D. A. Cooper.—p. 105.
Biology of Ageing. E. A. Bortz.—p. 112.
Review of Basic Psychiatric Principles. P. J. Poinsard.—p. 116.
Post-Prandial Blood Sugar: A Probable Normal. J. L. Ackerman and E. M. Bohan.—p. 122.
*Mesenteric Vascular Occlusion. C. J. Dougherty.—p. 125.

Mesenteric Vascular Occlusion.—The symptomatology of the patient here discussed resembled that of acute appendicitis. The symptoms did not include the sudden severe abdominal pain with shock and collapse seen in a complete occlusion of a large mesenteric vessel with extensive devitalization of bowel. The pain was at first diffuse throughout the abdomen. Nausea was present, but vomiting was minimal, and the pain did not become severe until the day of admission. Laboratory studies indicated an infectious process; there was a high white cell count, and the urinary findings could be interpreted as the reaction of the kidneys to the toxemia. Serum amylase studies were not done prior to the emergency laparotomy, because the site of the tenderness and rigidity did not suggest acute pancreatitis. Mesenteric occlusion, a volvulus of the cecum or small bowel, and perforated Meckel's diverticulum could have been considered preoperatively as possibilities, but the commoner diseases are usually thought of in the presence of acute abdominal symptoms. The gangrenous portions of the terminal ileum and cecum were resected, and a temporary ileostomy was made. After the intestinal continuity was reestablished in a second operation, the patient recovered from this often fatal disease.

Florida Medical Association Journal, Jacksonville

38:1-76 (July) 1951

Massive Resection of Small Intestine: Follow-Up Study of Case After Removal of 12 Feet Six Inches of Small Intestine. J. C. Pate and J. C. Pate Jr.—p. 19.
Perforation of Gastric and Duodenal Ulcers: Analysis of 63 Cases at Duval Medical Center. E. Jelks and C. M. Collins.—p. 23.
Insulins and Their Uses. S. Davidson.—p. 30.
The Cervical Stump—Necessary Evil? J. P. Michaels.—p. 35.
General Practice and Urology with Commentary on Educational Trends in Medicine, Past and Present. J. F. McCarthy.—p. 38.

Georgia Medical Association Journal, Atlanta

40:239-278 (June) 1951

Spontaneous Pneumothorax. G. R. Dillinger.—p. 239.
Significance and Management of Peripheral Pulmonary Masses. O. A. Abbott, W. A. Hopkins, T. F. Leigh and W. E. VanFleit.—p. 243.
Clinical Recognition and Treatment of Pulmonary Embolism and Its Prodromes. H. N. Hill.—p. 250.
Chloromycetin Treatment of Typhoid Fever. D. F. Mullins Jr. and W. H. Bonner.—p. 254.
Basic Concepts of Allergic Disease. E. R. Cook III.—p. 255.

G.P. (J. Am. Acad. Gen. Practice), Kansas City, Mo.

3:1-192 (June) 1951

Painful Syndromes. W. M. Craig.—p. 32.
Eczema and Asthma in Children. B. Ratner.—p. 39.
Helping the Child with Delayed Speech. S. S. Hawk.—p. 43.
Radiotherapy in Malignant Disease. D. H. Allen.—p. 50.
Major Amputations. D. B. Slocum.—p. 55.
Treatment of Rheumatoid Arthritis. R. T. Smith.—p. 66.

Journal of Clinical Investigation, Cincinnati

30:539-684 (June) 1951

*Peripheral Vascular Hemodynamics in Bulbar Conjunctiva of Subjects with Hypertensive Vascular Disease. R. E. Lee and E. A. Holze.—p. 539.
Sensitivity of Serum Enzyme Inhibitors to Variety of Cancer Chemotherapeutic Agents. F. W. Ellis and P. M. West.—p. 547.
Estimation of Total Body Sodium by Isotopic Dilution: I. Studies on Young Adults. G. B. Forbes and A. Perley.—p. 558.
Id.: II. Studies on Infants and Children: Example of Constant Differential Growth Ratio. G. B. Forbes and A. Perley.—p. 566.
Immunophysiology of Trichinosis: Alterations in Blood Volume and Thiocyanate Space in Relation to Development of Humoral Antibodies in Rabbit. J. K. Aikawa, G. T. Harrell and T. B. Miller.—p. 575.
Bacterial Capsular Polysaccharides in Cerebrospinal Fluid of Patients with Purulent Meningitis. D. L. Larson.—p. 582.
Dietary Treatment of Hypertension: II. Sodium Depletion as Related to Therapeutic Effect. V. P. Dole, L. K. Dahl, G. C. Cotzias and others.—p. 584.
Congenital SPCA Deficiency: Hitherto Unrecognized Coagulation Defect with Hemorrhage Rectified by Serum and Serum Fractions. B. Alexander, R. Goldstein, G. Landwehr and C. D. Cook.—p. 596.
Plasma Proteins in Toxemias of Pregnancy. H. C. Mack, A. R. Robinson, M. E. Wiseman and others.—p. 609.
Measurement of C-Reactive Protein in Human Sera: Comparison of Clinical Tests on Basis of Quantitative Method. H. F. Wood and M. McCarty.—p. 616.

Hemodynamics in Bulbar Conjunctiva in Hypertension.—Studies were made on the conjunctival capillary vessels of subjects with hypertensive vascular disease. The bulbar conjunctiva in each eye was examined with a slit-lamp microscope in a manner similar to that used in routine ophthalmological practice. The general state of the capillary bed was noted (i. e., ischemic, plethoric, or euvascular). In certain cases, the velocity of blood flow was measured in the metarterioles, capillaries, and collecting venules. The capillary bed and its reactions in the conjunctiva of normotensive subjects had been previously described. When all criteria selected for evaluation were considered together, an over-all pattern emerged of certain peripheral vascular abnormalities in hypertension. The total pattern was not found in the normotensive controls. However, no one feature selected for study could be correlated absolutely with the age of the patient, the degree of blood pressure elevation, symptomatology, or the duration of the illness. The abnormal hemodynamics observed in the conjunctival peripheral circulation in essential hypertension consisted of: (1) metarteriolar narrowing, (2) augmented spontaneous vasomotor activity in precapillary sphincters, and (3) coiling, looping, and tortuosity of many vessels. There was also a heightened sensitivity of metarterioles and precapillaries to topically applied epinephrine, and a reduced velocity of peripheral blood flow. These features are generally in accord with those that have been described for similar vessels in the splanchnic area of animals with experimental renal hypertension. The conjunctival peripheral vessels of four normotensive subjects who had had an apparently spontaneous remission of previous hypertension displayed the same phenomena found in the conjunctival vascular bed of patients with sustained hypertension.

Journal of Experimental Medicine, New York

93:513-654 (June) 1951

Antimicrobial Agents in Prevention of Dietary Hepatic Injury (Necrosis, Cirrhosis) in Rats. P. György, J. Stokes Jr., H. Goldblatt and H. Popper.—p. 513.
Studies on Immunity in Anthrax: II. In Vitro Elaboration of Protective Antigen by Non-Proteolytic Mutants of Bacillus Anthracis. G. G. Wright, M. A. Hedberg and R. J. Feinberg.—p. 523.
Endocrines and Their Relation to Influenza Virus Infection. S. S. Kalter, H. J. Smolin, J. M. McElhaney and J. Tepperman.—p. 529.
Conversion of Plasma Protein to Tissue Protein Without Evidence of Protein Breakdown: Results of Giving Plasma Protein Labeled with $Carbon^{14}$ Parenterally to Dogs. C. L. Yuile, B. G. Lamson, L. L. Miller and G. H. Whipple.—p. 539.
Variability of BCG Strains (Bacillus Calmette-Guérin). W. E. Suter and R. J. Dubos.—p. 559.
Nature and Significance of Changes in Adrenal Cytology, Weight, and Cortical/Medullary Ratio in Experimental Renal Hypertension and Clinical Hypertension. L. J. Rather.—p. 573.
New Member of Psittacosis-Lymphogranuloma Group of Viruses that Causes Infection in Calves. C. J. York and J. A. Baker.—p. 587.
Mechanism of Proteinuria: IV. Effect of Renin on Hemoglobin Excretion. R. W. Lippman, H. J. Ureen and J. Oliver.—p. 605.
Studies on Acute Disseminated Encephalomyelitis Produced Experimentally in Rhesus Monkeys: VI. Changes in Cerebrospinal Fluid Proteins. E. A. Kabat, A. Wolf, A. E. Bezer and J. P. Murray.—p. 615.
Relation of Krebs Cycle to Viral Synthesis: II. Effect of Sodium Fluoroacetate on Propagation of Influenza Virus in Mice. W. W. Ackermann.—p. 635.

Journal of Immunology, Baltimore

66:487-626 (May) 1951

Experimental Production of Arteritis by Passive Sensitization. S. G. Cohen, L. D. Mayer and L. H. Criep.—p. 487.
Serological Identification of Cultures of Clostridium Sporogenes. J. W. Mandia and D. W. Bruner.—p. 497.
Hemolysis Inhibition Test for Detection of Antibodies to Newcastle Disease Virus. M. J. Kahnke.—p. 507.
Field Trial of Shigella Flexneri III Vaccine: VI. Mouse Protective Studies. L. A. Barnes, M. L. Cooper, E. A. Jerome and others.—p. 515.
Effect of X Rays upon Hemolysin Production in Rat. H. I. Kohn.—p. 525.
Studies on Prevention of Mumps: I. Determination of Susceptibility. G. Henle, W. Henle, J. S. Burgoon and others.—p. 535.
Id.: II. Effect of Skin Testing upon Antibody Level and Resistance. G. Henle, J. S. Burgoon, W. J. Bashe Jr. and others.—p. 551.
*Id.: III. Effect of Subcutaneous Injection of Inactivated Mumps Virus Vaccines. G. Henle, W. J. Bashe Jr., J. S. Burgoon and others.—p. 561.
*Id.: IV. Effect of Oral Spraying of Attenuated Active Virus. G. Henle, J. Stokes Jr., J. S. Burgoon and others.—p. 579.
Experimental Human Salmoneliosis: II. Immunity Studies Following Experimental Illness with Salmonella Meleagridis and Salmonella Anatum. N. B. McCullough and C. W. Eskelo.—p 595.
Nature of Combining Sites of Antibodies: Specific Protection of Combining Site by Hapten During Iodination. D. Pressman and L. A. Sternberger.—p. 609.
Effects of Cortisone and ACTH on Toxins of Rickettsiae and Salmonella Typhosa. E. B. Jackson and J. E. Smadel.—p. 621.

Subcutaneous Injection of Mumps Virus Vaccines.—A large part of the studies reported here were carried out in Southeastern Alaska, where there had been no major epidemic of mumps for over eight years. Consequently, it was expected to find many persons in older age ranges who never had been exposed to mumps and thus the antibody response in truly susceptible individuals could be studied. The serological response of human beings to subcutaneous vaccination with inactivated mumps virus, as measured by complement fixation and hemagglutination inhibition tests, was studied. Maximal complement-fixing antibody response was obtained two to three weeks after vaccination. A single injection of vaccine resulted in antibody responses indistinguishable from those recorded after two injections two weeks apart. The frequency of response, as well as the height of titers attained, depended on the amount of vaccine injected. Only with 4 ml. of vaccine, representing approximately a 20-fold concentrate of virus from allantoic fluid, did all susceptible persons show some antibody response. A correlation between the antibody titers obtained by the virus antigen complement-fixation test, and those obtained by the hemagglutination-inhibition reaction, indicated that the two techniques probably measure different antibodies. Although, in general, a high titer by one test was matched by a high antibody level in the other, the ratios of hemagglutination-inhibition to complement-fixation titers varied over a range far greater than could be ascribed to the variations inherent in the techniques. An epidemic of mumps occurred nine to 12 months after vaccination. The incidence of infection among the controls (63 cases in 193) was almost twice that encountered in the immunized group (46 cases in 250). This result gained in significance when the incidence of mumps in the vaccinated group was correlated with the antibody levels attained four to five weeks after vaccination. The incidence was highest in those who failed to respond with measurable antibodies to vaccination and decreased markedly with the increase in the antibody level attained after immunization. The data indicate that transitory immunity may be induced by subcutaneous vaccination with inactivated mumps virus and that its duration seems to be related to the height of antibody levels attained.

Oral Spraying of Mumps Virus.—Studies on the response of human beings to oral spraying of attenuated active mumps virus revealed that among 410 children judged susceptible by negative histories and serological tests, six showed mild signs of infection. Up to 93% of the children responded with antibodies as measured by the complement-fixation technique. The frequency of response depended on the concentration of virus used. Hemagglutination-inhibition tests in a small number of cases revealed formation of antibodies in 60%. In most instances the serological tests were negative one year after the spraying. However, following skin testing at that time, the antibody response was greater in these children than in comparable control subjects. Experimental exposure of four children to mumps virus three months after immunization failed to produce the disease, whereas in four out of six controls clinical evidence of mumps developed. Of the larger groups treated by this procedure only those in one institution had been definitely exposed to mumps eight months later. Eight cases occurred among the nonimmunized children, mainly new admissions to the school. Although these data permit no conclusion, they justify further exploration of this method of active immunization.

Journal of International College of Surgeons, Chicago

16:1-140 (July) 1951

Surgical Treatment of Some Cardiovascular Diseases (New Vascular Anastomosis). C. A. Carlon, P. G. Mondini and R. De Marchi.—p. 1.
Cardioesophageal Surgery. E. J. Borges.—p 12.
Meckel's Diverticulum. S. J. Carnazzo and E. J. McGreevy.—p. 22.
Prolapse of Uterus: Operation for Its Relief. A. E. Kanter, A. H. Klawans and R. W. Hack.—p. 37.
*Myoepithelial Hamartoma of Stomach Wall. M. Thorek.—p. 48.
Surgical Approach to Glaucoma. D. T. Atkinson.—p. 58.
Preoperative and Postoperative Care in Gastric Surgery. S. H. Babington.—p. 73.
*Treatment of Trichomonas Vaginalis Vaginitis: II. Factors Affecting Response to Treatment. W. J. Reich, H. L. Button and M. J. Nechtow.—p. 86.
Compression Fixation Arthrodesis of Knee. A. A. Michele and F. J. Krueger.—p. 93.
Estradiol Implants in Postoperative Pituitary Exophthalmos. M. V. Okie, H. B. Denee and W. Daley.—p. 98.
Surgical Aspects of Meckel's Diverticulum. A. B. McGraw.—p. 101.
Gallstones in Stomach Wall with Symptoms of Pyloric Stenosis: Report of Case. H. Z. Konuralp.—p. 105.
Perforation of Gallbladder. J. P. Cangelosi, A. L. Vincenti and E. Kalvelage.—p. 110.

Myoepithelial Hamartoma of Stomach Wall.—This case concerns a man, 47, with pain in the epigastric region of two years' duration, not related to the ingestion of food but aggravated by alcoholic beverages. Roentgenograms taken at the onset of the disease revealed no abnormality, but a second roentgen examination shortly before the patient's admission to the hospital showed a filling defect in the antral portion of the stomach. Physical and laboratory examinations gave no definite information. Subtotal gastric resection permitted the removal of a mass in the antral portion of the stomach. On section this mass showed islands of pancreatic acini and many ductlike structures. The final diagnosis was myoepithelial hamartoma of the stomach. The exact cause of the lesion is not known. The fact that accurate diagnosis can never be reached except by microscopic examination of tissue obtained either at operation or autopsy makes it imperative for the general practitioner to be aware of the possibility of "aberrant pancreas" as a cause of some obscure gastrointestinal manifestations that cannot be readily classified.

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Trichomonas Vaginitis.—Of 325 patients with Trichomonas vaginalis vaginitis, 158 were treated by nightly insertion in the vagina of capsules of 4 gm. of argypulvis® (finely powdered mild silver protein [argyrol®], kaolin, and lactose) and 194 were given capsules containing 2 gm. of argypulvis.® The capsules were inserted in the vagina after a preliminary douche with four tablespoonfuls of white vinegar in two quarts of warm water to make certain that there was adequate moisture. The treatment proved effective in all but five patients. Three of the failures occurred in the group who had received 4 gm. argypulvis® capsules, and in two of those who received 2 gm. capsules. Thus the 2 gm. dose was as effective as the 4 gm. dose. Three and probably four of the therapeutic failures were associated with a history of recent supracervical hysterectomy. It is possible that a resistant trichomonad focus was created in the persisting cervical stump. All the failures occurred in patients between 25 and 39, with a vaginal pH below 6 at the start of therapy. Simple correction of the vaginal pH to normal may not be relied on to eliminate the trichomonal infection, since the vaginal pH was within the normal range in some of the most resistant of the authors' cases. Some recurrences were observed after 17 to 42 weeks, over which the patients remained Trichomonas-negative. There can be no doubt that the marriage partner contributes to this type of recurrence; several instances of trichomonads in the male were observed in the prostatic secretion, the urine, or the seminal fluid. Complete success in the treatment of Trichomonas vaginitis can be obtained only through complete awareness of all the factors contributing to its persistence and recurrence.

Journal Lab. and Clinical Medicine, St. Louis

37:831-992 (June) 1951

Porphyrin Chromogens or Precursors in Urine, Blood, Bile, and Feces. C. J. Watson, R. Pimenta de Mello, S. Schwartz and others.—p. 831.

Improved Method for Determination of Urinary Coproporphyrin and Evaluation of Factors Influencing Analysis. S. Schwartz, L. Zieve and C. J. Watson.—p. 843.

Acetylcholine and Cholinesterase in Blood of Patients Suffering with Bronchial Asthma. H. H. Scudamore, L. J. Vorhaus and R. M. Kark.—p. 860.

Artifactual Values of Serum Precipitable Iodine After Clinical Intramuscular Injections of Mercuhydrin. J. H. Meyers and E. B. Man.—p. 867.

Observations on Effect of Cortisone Acetate on Two Patients with Hepatic Disease. H. R. Butt, M. W. Comfort, M. H. Power and H. L. Mason.—p. 870.

Photochromatographic Analysis of Amino Acids in Body Fluids: Method and Some Applications. A. A. Albanese, R. A. Higgons, B Vestal and L. Stephanson.—p. 885.

Qualitative and Quantitative Changes in Plasma Proteins of Lipoid Nephrosis Demonstrated by Electrophoresis. M. A. Fischer, P. A. Steinman, A. M. Carpenter and M. L. Menten.—p. 894.

Effects of Potassium Chloride on Intestinal Motility in Human Beings and Dogs. P. C. Gazes, J. A. Richardson and M. deV. Cotten.—p. 902.

Zirconium Treatment in Ivy Poisoning: Preliminary Investigation. G. A. Cronk and D. E. Naumann.—p. 909.

Identification of Influenza Virus Antibodies by Means of Collodion Particle Agglutination Reaction. A. V. Boand and J. E. Kempf.—p. 914.

Protection of Intracellular Brucella Against Streptomycin Alone and in Combination with Other Antibiotics. R. L. Magoffin and W. W. Spink.—p. 924.

Epidemic of Typhoid Fever at Spenard, Alaska. W. H. Gaub.—p. 931.

Reaction of Bone Marrow to High Oxygen Tension in Normal and Anemic Guinea Pigs. A. Cooperberg and K. Singer.—p. 936.

Journal of Nervous and Mental Disease, New York

113:471-566 (June) 1951

Certain Aspects of Sensory Organization of Human Brain: Study in Rostral Dominance as Determined by Ipsilateral Simultaneous Stimulation. R. Cohn.—p. 471.

Basal Electroencephalography: Some Findings. A. P. Arellano and P. D. Maclean.—p. 485.

Psychopathology of Acromegaly. M. Bleuler.—p. 497.

Experimental Investigation of Body-Mind Continuum in Affective States. B. Pasquarelli.—p. 512.

Ictal and Non-Ictal Psychiatric Disorders in Temporal Lobe Epilepsy. F. A. Gibbs.—p. 522.

Chemical Analysis of Spectrophotometric Findings in Cerebrospinal Fluid. M. Spiegel-Adolf, H. T. Wycis and E. A. Spiegel.—p. 529.

Blood Lymphocytes and Adrenal Function in Electric Convulsive Therapy of Psychoses. S. T. Michael and W. T. Brown.—p. 538.

Proc. Soc. Exper. Biol. & Med., Utica, N. Y.

77:1-192 (May) 1951. **Partial Index**

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Comparison of Leukocyte Response to ACTH and Bacterial Pyrogen. B. Soylemezoglu and J. A. Wells.—p. 43.

Anti-Tubercular Activity in Vivo of Nicotinaldehyde Thiosemicarbazone and Its Isomers. E. Grunberg and B. Leiwant.—p. 47.

Effect of ACTH and Cortisone on Homogenous Kidney Transplants. L. Persky and S. Jacob.—p. 66.

Response of Mice to Certain Avirulent Bacteria After Exposure to Sublethal Total Body X-Irradiation. I. L. Schechmeister and V. P. Bond.—p. 77.

Renal Clearance of Endogenous Phosphate in Infants and Children. J. B. Richmond, H. Kravitz, W. Segar and H. A. Waisman.—p. 83.

Fate and Excretion of Adrenocorticotrophic Hormone. J. B. Richards and G. Sayers.—p. 87.

Observations on Relationship Between Vitamin B_{12}, Folic Acid and Citrovorum Factor. L. S. Dietrich, W. J. Monson and C. A. Elvehjem.—p. 93.

Essential Amino Acids in Mature Human Milk. S. Miller and V. Ruttinger.—p. 96.

Effects of Modified Human Globin in Normal Human Subjects. J. L. Brandt, A. Caccese and V. Ginsberg.—p. 108.

*Relationship Between Epidemic Keratoconjunctivitis and St. Louis Encephalitis Viruses. I. Ruchman.—p. 120.

*Possible Relationship Between Viruses of St. Louis Encephalitis and Epidemic Keratoconjunctivitis. F. S. Cheever.—p. 125.

Resistance of Red Cells to Dialuric Acid of Premature Infants with Retrolental Fibroplasia. S. Cohen, J. P. DeMetry and H. Herrmann.—p. 134.

Lethal Infection with Coxsackie Virus of Adult Mice Given Cortisone. E. D. Kilbourne and F. L. Horsfall Jr.—p. 135.

Negative Effects of Vitamin B_{12} on Blood of Healthy Individuals, with Special Reference to Eosinophils. R. C. Muehrcke and R. M. Kark.—p. 144.

Histoplasma Capsulatum in Tissue Culture. C. C. Randall and D. L. McVickar.—p. 150.

*Depression of Fecal Urobilinogen by Aureomycin and by Terramycin. W. C. Robbins.—p. 158.

*In Vitro and in Vivo Studies of New Antibiotic, Fumagillin, with Endamoeba Histolytica. A. K. Hrenoff and M. Nakamura.—p. 162.

Viruses of Epidemic Keratoconjunctivitis and St. Louis Encephalomyelitis.—Ruchman's studies indicate that it is impossible at present to distinguish epidemic keratoconjunctivitis virus from St. Louis encephalitis virus by means of the intracerebral neutralization test in mice. The serums from animals convalescing from epidemic keratoconjunctivitis and from St. Louis encephalitis neutralized epidemic keratoconjunctivitis and St. Louis encephalitis viruses equally. No differences could be elicited by neutralization tests with the keratoconjunctivitis virus that had been through three successive rabbit passages. Neutralization tests in which serum dilutions were used against a constant amount of virus also failed to show differences between the two viruses. Significant cross-neutralization was obtained with the related Japanese B and West Nile viruses. Infectivity tests in animals revealed that rabbits and guinea pigs were susceptible to intracerebral inoculation with keratoconjunctivitis virus but not to St. Louis virus. The studies described by Cheever give evidence confirming Ruchman's observations that the viruses of St. Louis encephalitis and epidemic keratoconjunctivitis are closely related. He stresses the importance of careful study of current outbreaks of epidemic keratoconjunctivitis as a means of assessing the significance of these findings.

Depression of Fecal Urobilinogen by Aureomycin and Terramycin.—Robbins shows that the oral administration of aureomycin or terramycin to man results in an extremely low concentration of fecal urobilinogen. This change occurs during the first 48 to 72 hours of therapy, concurrently with other modifications in the intestinal contents. Normal concentrations of urobilinogen may not be restored for six or seven days after the discontinuance of drug administration. The depression of urobilinogen formation is probably the result of alterations in the flora of the intestine. A case of hemolytic anemia is reported in which strikingly low fecal and urinary urobilinogen concentrations were observed while the patient was receiving aureomycin.

Fumagillin Against Amebiasis.—A new antibiotic, designated "antibiotic H-3" or fumagillin, has been isolated from Aspergillus fumigatus. Studies in vitro and in vivo demonstrated that it has amebacidal properties. This paper is a report of studies

undertaken to determine the in vitro effectiveness of this new antibiotic, with some preliminary observations relative to the treatment of macaques infected with Endamoeba histolytica. Fumagillin was found to be effective in vitro against E. histolytica at concentrations of 1: 10,000,000 to 1: 15,000,000. Preliminary in vivo studies on monkeys naturally infected with E. histolytica indicated that fumagillin possesses significant amebacidal activity.

Psychiatric Quarterly, Utica, N. Y.

25:201-378 (April) 1951

Future Organization of Psychiatric Care. P. V. Lemkau.—p. 201.
Some Physiologic Common Denominators of Histamine, Sex Steroids, Insulin and Electric Convulsive Therapies. M. D. Sackler, R. R. Sackler, A. M. Sackler and others.—p. 213.
Psychiatric Aspects of Asthma. C. T. Prout.—p. 237.
Thalamo-Cingulate Fasciculotomy. J. H. Siris.—p. 251.
Fiction of Death Instinct. A. J. Levin.—p. 257.
Relation of Rh to Mental Deficiency. F. B. Glasser, M. Jacobs and R. Schain.—p. 282.
Emotional Reactions of Schizophrenic Patient to Shock Therapy. M. L. Hayward.—p. 289.
Schizophrenic Reactions During Childhood in Mental Defectives. M. Bergman, H. Waller and J. Marchand.—p. 294.

Psychosomatic Medicine, New York

13:133-210 (May-June) 1951

Life Situations, Emotions, and Course of Patients with Arterial Hypertension. M. F. Reiser, A. A. Brust and E. B. Ferris.—p. 133.
Relationship Therapy in Essential Hypertension: Psychosomatic Conference of Cincinnati General Hospital. A. P. Shapiro, M. Rosenbaum and E. B. Ferris.—p. 140.
Psychologic Mechanisms in Malignant Hypertension. M. F Reiser, M. Rosenbaum and E. B. Ferris.—p. 147.
Studies in Diabetes Mellitus. L. E. Hinkle Jr., F. M. Evans and S. Wolf. —p. 160.

South Carolina Medical Assn. Journal, Florence

47:187-228 (June) 1951

*Anaphylactic Shock from Wasp Stings. W. H. Williams Jr.—p. 187.
Carcinoma of Cervical Stump. H. C. Heins and H. R. Pratt-Thomas. —p. 192.
Office Gynecology. D. F. Watson.—p. 196.
Submaxillary Duct Calculi. A. M. Stanton, F. T. Wallace and W. F. Utterman.—p. 201.

Anaphylactic Shock from Wasp Stings.—Williams reviews the literature on severe general and fatal reactions due to anaphylaxis from bee and wasp stings and presents the case of a man who had been stung on the left hand and forearm by six or seven wasps. He began to "itch all over," became extremely weak and nervous, "frothed at the mouth," and collapsed within 15 minutes after the stings. On admission to the hospital he was cyanotic and covered with perspiration and his blood pressure could not be obtained or pulsations felt at the wrist. There was tachycardia. Breathing was rapid, shallow, and stertorous, and the general appearance was that of a patient with a cerebrovascular accident. The man was immediately given 1 cc. of epinephrine subcutaneously, then 50 mg. of diphenhydramine (benadryl*) hydrochloride intravenously. Administration of oxygen by mask was started, followed by intravenously administered glucose in saline solution and blood. This treatment caused a slight improvement, in that the blood pressure could be registered. The patient was irrational and violent and had to be restrained; he was given amobarbital (amytal*) sodium and morphine and scopolamine. On the fourth day the patient still required oxygen as well as restraints and sedation. Then cortisone was started in 100 mg. doses at eight-hour intervals for three doses. After this, great improvement could be seen. It is believed that the cortisone was life-saving, but it is also suggested that the patient might have responded more promptly had more epinephrine been given. The use of epinephrine in adequate doses, antihistaminic agents, and general shock-combating measures is recommended as immediate first aid, to be followed by cortisone or, preferably, corticotrophin in cases of anaphylaxis.

Southern Medical Journal, Birmingham, Ala.

44:571-672 (July) 1951

Cirrhosis: A Dynamic Disease. J. S. Levy, A. G. Kahn Jr. and R. W. Talley.—p. 571.
Critical Evaluation of Therapy in Cirrhosis of Liver. W. D. Davis Jr. —p. 577.
New Technic for Transvesical Surgery. J. C. Alexander, K. B. King and F. Fuqua.—p. 580.
Radiographic Findings in Protruded Cervical Discs. R. D. Moreton and G. Ehni.—p. 582.
Oil Soluble Anesthetics in Proctology. A. M. Phillips.—p. 588.
Transfusion in Management of Closed Head Injury: Preliminary Report. E. A. Smolik, S. Brown and F. P. Nash.—p. 592.
Posttraumatic Ischemic Infarction of Kidney Due to Arteriospasm: Clinicopathological and Experimental Study. K. M. Lynch Jr. and H. L. Large Jr.—p. 600.
Clinical Evaluation of Antacid Therapy in Treatment of Peptic Ulcer Syndrome. V. Moseley and W. G. Coker Jr.—p. 610.
Ringworm of Scalp: Treatment with Tetrachloro-Para-Benzoquinone: Clinical and Laboratory Analysis. J. L. Rankin, W. L. Dobes, J. W. Jones and H. S. Alden.—p. 616.
Treatment of Lateral Deviations. W. W. Sanger.—p. 620.
Periarteritis Nodosa Treated with ACTH: Report of Case. B. F. Martin. —p. 626.
Analysis of Clinical Data on 500 Childless Couples: Fertility Results. V. H. Turner, C. D. Davis, J. Zanartu and E. C. Hamblen.—p. 628.
High Fluid Intake in Treatment of Eclampsia: Report of 25 Cases. F. E. Whitacre and O. DeLozier.—p. 638.
Two-Year School in Modern Medical Education. T. H. Stubbs.—p. 643.
Radioactive Iodine Therapy of Hyperthyroidism: Determination of Optimum Dosage. B. J. Sweeney, W. H. Daughaday, L. Gotlieb and others.—p. 648.
Significance of Radiosodium Space in Human Disease: Comparison with Thiocyanate Space. J. K. Aikawa.—p. 654.
*Use of Hyaluronidase in Chronic Ulcers: Preliminary Report. M. Ende. —p. 661.

Hyaluronidase in Chronic Ulcers.—Since one of the causes of chronic ulcers is inadequate nutrition to the tissues, Ende felt that hyaluronidase might facilitate passage of necessary agents into an ulcerated area and thereby promote healing. The first patient in whom hyaluronidase was used was a man, 25, who in childhood had had osteomyelitis in the left leg. In June, 1950, an ulcer developed 3 in. (7.62 cm.) by 1¾ in. (4.45 cm.) and approximately ¼ in. (0.64 cm.) in depth. The patient was treated for several months with penicillin and local applications. He was then put on bed rest, and penicillin was continued for 10 days. The ulcer did not heal. Penicillin was stopped, and bed rest continued. One ampule of 400 viscosity units of hyaluronidase dissolved in 1 cc. of water was applied to the lesion daily. The patient noted significant relief of pain in 24 hours. Within one week the ulcer was approximately half its original size, and it healed in three weeks. The second patient was a woman, 65, who had had leg ulcers for 40 years. One ulcer covered an area 5½ in. (13.97 cm.) by 4½ in. (11.43 cm.), a smaller one measured 1 in. (2.54 cm.) by 1½ in. (3.31 cm.). This smaller ulcer healed under treatment with hyaluronidase in four weeks; the larger ulcer was reduced in size and granulated to the level of the skin in two and one half months. It is ready for skin grafting. Similar favorable results were obtained in a third patient. All three had rapid diminution in pain. Ende feels that further investigation of the use of the drug in wound-healing is indicated.

Texas State Journal of Medicine, Fort Worth

47:319-456 (June) 1951

Medicine's Modern Problems. W. M. Gambrell.—p. 324.
In Memoriam: Tribute to Deceased Doctors. O. N. Mayo.—p. 327.
Communist Threat to America. M. Dies.—p. 328.
Facial Palsies: Indications for Their Surgical Repair. J. E. Witcher. —p. 336.
Cervical Spine Injuries. J. E. Watson Jr.—p. 341.

West Virginia Medical Journal, Charleston

47:169-196 (June) 1951

Breech Presentation. R. T. Rapp.—p. 169.
Pneumoperitoneum in the Newborn. M. Birdsong and E. M. Frame. —p. 173.
Relation of Public Health Department to Private Practice of Medicine. R. A. Kennedy.—p. 177.
Diagnosis and Treatment of Renal Tumors. G. A. Humphreys.—p. 180.
Choice of Medical Students with Especial Reference to Nature and Usefulness of the Medical College Admission Test. G. S. Dodds and E. J. Van Liere.—p. 184.
Chylous Ascites (Report of Case). R. E. Burger.—p. 186.

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Acta Physiologica Scandinavica, Stockholm

22:299-390 (No. 4) 1951. **Partial Index**

Substances Affording Partial Protection Against Certain Vitamin E Deficiency Symptoms. H. Dam, I. Kruse, I. Prange and E. Søndergaard.—p. 299.
*Quantitative Study on Alcohol-Barbiturate Synergism. F. Sandberg. —p. 311.
Effect of Trichlorethylene on Organism. A. Ahlmark and S. Forssman. —p. 326.
Disappearance of Injected Histamine from Blood Stream. N. Emmelin. —p. 379.

Alcohol-Barbiturate Synergism. — Sandberg's studies demonstrate that small, subhypnotic doses of several short-acting barbiturates produce a marked potentiation of the effect of alcohol measured by the diminished induction time of anesthesia. The degree of potentiation varied with the dose and the type of barbiturate derivative. Hexobarbital was found to produce the highest degree of synergism, followed by 1-carbethoxymethyl-5, 5-diallylbarbituric acid, amobarbital, thiopental, and cyclobarbital. A test has been developed for the analysis of the differences in the degree of potentiation. No correlation is found between the degree of potentiation and hypnotic efficiency or induction time. Sandberg believes that discrepancies between his observations and those of observers who noted a retarding effect of alcohol on the anesthesia induced by barbiturates may be due to the differences between short-acting and long-acting barbiturates. The clinical use of the combination of alcohol and a short-acting barbiturate was reported by Rachek in 1945, who stated that the synergistic action of alcohol and hexobarbital has been utilized to advantage in intravenous anesthesia. The present investigation indicates that a potentiative, not a simple additive, type of synergism exists between alcohol and the short-acting barbiturates and that the degree of potentiation varies with the dose and the type of the barbiturate derivative.

British Medical Journal, London

1:1405-1462 (June 23) 1951

Some Impressions of an Ophthalmologist. A. W. S. Sichel.—p. 1405.
Aspects of Circulation's Economy. K. J. Franklin.—p. 1410.
Suicide Statistics. D. Swinscow.—p. 1417.
*Antihistamine Treatment of Acute Nephritis. D. Lawson.—p. 1423.
Treatment of Psychoneurosis: Modified CO_2 Abreactive Technique. W. L. Milligan.—p. 1426.
*Idiosyncrasy to Aureomycin. P. D. Bedford.—p. 1428.
New Diluting Fluid for Eosinophil Count. T. Manners.—p. 1429.

Antihistamine Treatment of Acute Nephritis.—Since most cases of acute nephritis follow a bacterial, usually a streptococcic infection by one to three weeks, it has been widely accepted that immunity responses are involved in the pathogenesis of the disease. The known mediation of histamine or a histaminelike substance as a final common path in the production of a variety of hypersensitivity phenomena suggested a trial of one of the recently developed antihistamine drugs in the treatment of acute nephritis. Some investigators obtained encouraging results with pyranisamine maleate ("anthisan") in the treatment of eight cases of acute nephritis. Lawson tried this drug in the treatment of 33 consecutive cases of acute nephritis, alternate patients being treated with an antihistamine drug for 10 days. Cases were followed for from six and 18 months. This is a report on the first six months' experience, during which period every child except one recovered completely. Analysis of the total duration of activity shows that the patients treated with pyranisamine were consistently slightly slower in recovering. The report did not confirm the value of this agent in the management of acute nephritis. Lawson feels that in a series like this, in which every child but one recovered within a few weeks or months, it is not possible to study the effect of the drug on the long-term prognosis.

Idiosyncrasy to Aureomycin.—The patient showed sensitivity to acetylsalicylic acid (nausea, vomiting, and urticaria) and penicillin (eczematous dermatitis). Despite the known sensitivity to penicillin, he had been given 1,500,000 units of penicillin, under a heavy "umbrella" of antihistaminics and ephedrine, for cellulitis of the face. About four weeks later he was given 1 gm. of aureomycin by mouth for influenza with fever and a cough productive of purulent sputum. Ten minutes later he noticed itching of the groin and between the outer toes of both feet, sites which had been infected with ringworm some years previously. Two to three minutes afterward dyspnea developed, accompanied by stridor and cyanosis. The eyes protruded and the face became purple. A crowing inspiration ended the inspiratory difficulty, which was succeeded by a typical asthmatic attack that subsided spontaneously after two hours. Edema (a confluent urticaria) of the scrotum, hands, feet, and face reached maximum about two hours afterward and slowly subsided about 36 hours later. The view that this alarming episode was due to aureomycin was strengthened by a strongly positive skin test. There is possibly an antigenic relationship between the products of growth of various molds and fungi. Though they may be uncommon, severe reactions to the newer antibiotics should be anticipated, particularly in persons known to be sensitive to penicillin.

Canadian Journal of Medical Sciences, Ottawa

29:79-150 (June) 1951. **Partial Index**

Effects of High Doses of Amytal on Skeletal Muscle. B. E. Riedel and M. J. Huston.—p. 79.
Method for Estimating Rates of Gastric Secretion and Emptying. J. A. Hildes and D. L. Dunlop.—p. 83.
Peripheral Circulation and Epinephrine and Norepinephrine Content of Adrenals of White Rats Exposed to Cold. A. Des Marais and L. P. Dugal.—p. 90.
Influence of Oral Ascorbic Acid Administration on Adrenal Cortical Response to ACTH. F. R. Skelton and C. Fortier.—p. 100.
Lactic Dehydrogenase Activity and Pyridine Nucleotide Content of Human Blood Cells in Anemia. M. C. Blanchaer, P. Weiss and D. E. Bergsagel.—p. 108.
Peptidase Activity in Human Serum Under Various Pathological Conditions, in Pregnancy, and Following Administration of ACTH. A. M. Cullen, V. T. Barber, M. K. Birmingham and K. Stern.—p. 114.
Effect of Ascorbic Acid on Experimental Nephritis. F. F. Howatt and P. W. Davey.—p. 124.

Edinburgh Medical Journal

58:197-260 (May) 1951

Applications of Chemical Defence Research in Medicine. R. A. Peters. —p. 197.
Social Aspects of Psychiatry: Part I. A. Lewis.—p. 214.
Id.: Part II. A. Lewis.—p. 231.
Tuberculosis in General Children's Hospital: Pathologist's Experience. A. R. Macgregor.—p. 248.

Hoja Tisiológica, Montevideo

11:1-108 (March) 1951. **Partial Index**

*Treatment of Metastases of Lung. A. Victorica.—p. 52.
*BCG Test in Children who Received BCG Vaccination at Birth. R. Gorlero Bacigalupi.—p. 60.

Treatment of Metastases of Lung.—According to Victorica, tumors that most frequently metastasize to the lung are, in order of frequency, carcinoma, sarcoma, chorionepithelioma, and tumors of the uterus, ovaries, and testicles. Symptoms of pulmonary metastases are the same as those of primary cancer of the lung. The roentgen aspects of the metastases are those of miliary nodules or of round or oval shadows. Biopsy and aspiration of bronchial secretion for identification of neoplastic cells are of diagnostic value. Pulmonary lobectomy is indicated when the metastases are solitary, when the primary tumor has been removed and the biopsy near the primary foci is negative for cancer, and when the general condition of the patient is satisfactory and the operation, as planned, should not greatly impair respiration. A patient is reported on whose left hand was amputated at its lower third because of sarcoma of the hand. Upper left lobe lobectomy was performed 20 months later for a single large metastasis of the lobe. The two carcinomas, that of the hand and of the lung, were of the same histological type. The patient is in good health and able to work six months after the operation.

BCG Test.—Gorlero Bacigalupi observed 770 children, of ages from birth to the age of 10 years who had had BCG vaccination at birth by the Rosenthal multipuncture technique. Skin puncture tests were made simultaneously in both forearms through a

drop of old tuberculin in one forearm and a drop of BCG vaccine in the other. Results, which were read 72 or 96 hours later, were positive with the BCG test in 701 cases (91.03%) and with the tuberculin test in 484 cases (62.85%). The hypoergic type of reaction was the same with either test. The percentage of positive reactions after vaccination increases from birth up to the age of 3 years and then gradually diminishes. The author concludes that with the BCG test there is a higher percentage of positivity and that, although the hypoergic responses predominate with both techniques, the responses to the BCG give a higher percentage of papules between 6 and 10 mm. in diameter. The results of these observations indicate the need to revaccinate children about three years after the first vaccination.

Journal of Clinical Pathology, London

4:129-252 (May) 1951

Whither Clinical Pathology? Trends and Opportunities. L. Whitby. —p. 129.
*Polyarteritis Nodosa and "Rheumatic" Diseases. W. Pagel.—p. 137.
Haemagglutination Reaction in Tuberculosis. G. R. F. Hilson and S. D. Elek.—p. 158.
Slide-Culture Technique for Determining Streptomycin Sensitivity of M. Tuberculosis in Sputum. S. D. Rubbo and D. M. Morris.—p. 173.
Determination of Sensitivity of Myco. Tuberculosis to Streptomycin. R. W. Fairbrother and J. E. Southall.—p. 183.
Proteolytic Enzyme Test for Detecting Incomplete Antibodies. J. A. Morton and M. M. Pickles.—p. 189.
Effect of Direct Electric Current on Normal and Antibody-Sensitized Red Cells. K. Goldsmith and J. G. Humble.—p. 200.
Effect of Citrovorum Factor (Folinic Acid) on Megaloblasts in Vitro. S. T. Callender and L. G. Lajtha.—p. 204.
Reticulocyte Crisis After Effective Specific Treatment of Pernicious Anaemia. R. Berlin.—p. 207.
Sampling Error in Haemoglobin Determination. R. Biggs and M. J. Allington.—p. 211.
Survival of Transfused Erythrocytes from Patients with Polycythaemia Vera. J. S. Elwood and H. E. de Wardener.—p. 218.
Combined Fragility Test for Congenital Haemolytic Jaundice. S. Varadi. —p. 221.
Estimation of Sodium Gentisate in Plasma and Urine. B. W. Meade and M. J. H. Smith.—p. 226.
Potassium Levels in Cerebrospinal Fluid After Death. J. K. Mason, W. Klyne and B. Lennox.—p. 231.

Polyarteritis Nodosa and Rheumatic Diseases.—Pagel tries to clarify the following points: (1) the early changes in polyarteritis nodosa and the question of the so-called fibrinoid substance; (2) some histological criteria reputed to distinguish polyarteritis nodosa from the rheumatic and "pararheumatic" diseases, including "temporal arteritis"; (3) polyarteritis nodosa as the basis of Löffler's syndrome associated with dermatoses; and (4) the causal role of bacterial hypersensitivity in polyarteritis nodosa. The studies reported were made on 18 cases. The early changes appear to be subendothelial swelling due to permeation of fluid, followed by fibrinogen exudation and necrosis of the vascular wall. A breach in the latter may be plugged by fibrin, or fibrin may be found both inside and outside the breached and necrotic vascular wall. Polyarteritis nodosa differs from the rheumatic and "pararheumatic" diseases (lupus erythematosus disseminatus, dermatomyositis, arteriolitis allergica, temporal arteritis) in its course and in the site and distribution of the lesions, but the basic histological change appears to be identical in all. In polyarteritis nodosa, fibrin deposition and necrosis affect the vascular walls mainly, but extramural foci may occur and involve the collagen fibers, with lesions indistinguishable from the acute "infiltrative" changes in rheumatic fever, lupus erythematosus disseminatus, and dermatomyositis. There is preservation of the argyrophil reticulin within the zone of collagen change. In addition to these paravascular foci, pseudotuberculous necrotic lesions may occur in polyarteritis nodosa. Finally, a granuloma resembling the Aschoff nodule and the changes seen in temporal arteritis may develop in the vascular wall. On the other hand, rheumatic arteritis, as seen in rheumatic fever, may be indistinguishable from polyarteritis nodosa and the vascular changes observed in dermatomyositis and scleroderma. Two cases are described of eosinophilic alveolitis in association with exfoliative dermatitis and asthma. In both there is evidence of burnt-out polyarteritis nodosa and of a "dissociation" of eosinophilia and arterial necrosis. The events that lead to the explosive arterial lesion of polyarteritis nodosa indicate a hyperergy. This hypersensitivity, which may involve a foreign or modified serum, or an abnormal protein, is comparable to the Arthus phenomenon and the type generally referred to as the anaphylactic type of allergy, but it may be due to a bacterial antigen, as shown by the use of streptococci in experiments on human volunteers.

Journal of Pathology and Bacteriology, Edinburgh

63:181-364 (April) 1951. **Partial Index**

Cardio-Vascular Responses to Air Embolism. G. R. Cameron, S. N. De and A. H. Sheikh.—p. 181.
Experimental Pulmonary Hypertension. C. V. Harrison.—p. 195.
*Intimal Vascularisation and Atherosclerosis. E. Geiringer.—p. 201.
Oedema and Capillary Anoxia. R. C. Nairn.—p. 213.
Myoneural Junctions and Toxic Agents. F. A. Denz.—p. 235.
Antidiuretic Hormone of Posterior Lobe of Human Hypophysis. C. Cavellero and M. Zanchi.—p. 249.
Retention of Radioactive Strontium and Yttrium (Sr^{89}, Sr^{90} and Y^{90}) in Pregnant and Lactating Rabbits and Their Offspring. B. Kidman, M. L. Tutt and J. M. Vaughan.—p. 253.
Observations on Resistance of Bacterium Coli to Glycine. J. Gordon, R. A. Hall and L. H. Stickland.—p. 285.
Beta-Toxin (Deoxyribonuclease) of Cl. Septicum. G. H. Warrack, E. Bidwell and C. L. Oakley.—p. 293.
Toxin-Producing Diphtheria-Like Organisms Isolated from Cases of Sore Throat. R. Saxholm.—p. 303.
Nasal Carrier Rates of Staphylococcus Pyogenes in Hospital Nurses. P. M. Rountree and R. G. H. Barbour.—p. 313.

Intimal Vascularization and Atherosclerosis.—Geiringer reviews the history of the study of atherosclerosis, giving particular attention to intimal vascularization and thrombogenic atherosclerosis. The material for his study was derived from routine autopsies at the Royal Infirmary in Edinburgh and consisted of 300 aortas taken in their entirety and sections from 100 hearts, including the first inch of the anterior descending branch of the left coronary artery. He stresses the following points: 1. The normal arterial intima is an avascular structure. 2. It acquires a secondary blood supply if it grows beyond a certain critical thickness. 3. This critical thickness, which varies with each artery, is about 0.5 mm. in the aorta and 0.35 mm. in the proximal part of the anterior descending branch of the left coronary. 4. Intimal vascularization occurs either through an extension of the adventitial plexus into and through the media or by retention of the vascular network of organizing mural thrombi. When both processes occur in the same vessel, anastomoses usually form. 5. This adventitious blood supply of the intima is liable to interference, and most of the clinical effects of atherosclerosis can be traced to the resulting ischemic necrosis of the intima. Living atherosclerotic thickenings are rarely a source of trouble. The vast majority of vascular accidents due to atherosclerosis occur in relation to necrotic plaques, and intimal vascularization is the forerunner of intimal necrosis.

Lancet, London

1:1331-1374 (June 23) 1951

Treatment of Psychoneurotics: Some Practical Considerations. W. L. Neustatter.—p. 1331.
Streptokinase as Adjunct in Treatment of Tuberculous Meningitis. J. Lorber.—p. 1334.
Induced Asthma in Man. H. Herxheimer.—p. 1337.
Primary Hydrocele and Its Treatment: Review of 200 Cases. D. P. Burkitt.—p. 1341.
Toxic Hepatitis Caused by Diaminodiphenylsulphone. D. B. Jelliffe. —p. 1343.
*Erysipeloid of Rosenbach: Review of 30 Cases. J. A. MacDougall. —p. 1345.
Cor Pulmonale from Recurrent Pulmonary Embolism. C. P. Petch. —p. 1346.
*Delayed Effects of Ultraviolet Burns in Man. M. L. Thomson.—p. 1347.
Gastro-Jejuno-Colic Fistula. C. C. Holman.—p. 1348.
Bullet Wound Through Both Frontal Lobes with Recovery. J. Slorach. —p. 1349.
In-Vivo Survival of Rabbit's Red Cell Recovered After Freezing. H. A. Sloviter.—p. 1350.

Erysipeloid of Rosenbach.—Erysipelothrix rhusiopathiae gives rise to three forms of infection in man: (1) a mild, localized cutaneous infection, (2) a diffuse or generalized cutaneous eruption with constitutional symptoms, and (3) a septicemic form. All of the 30 cases here reviewed fell into the first group. They were observed in the course of 10 months (1949/1950) at St. Thomas' Hospital in London. The part infected was the hand or fingers. The patients described a sensation of superficial itching or smarting, coupled with a feeling of tightness and stiffness of the under-

lying joints. The lesion was an erythematous patch spreading from the site of inoculation, varying from pink to deep purple, with a fairly distinct raised margin, and hot but not acutely tender. Three patients had systemic disturbances, with fever and malaise, and in one case, vomiting. All the patients were outpatients. No local application was given, but 28 patients were treated with the systemic administration of aqueous penicillin in doses of 200,000 or 500,000 units once or twice a day. The two patients who refused penicillin injections were left untreated, and the lesions resolved spontaneously, the first in 10 days and the second in 14. Of the 28 patients treated with penicillin, 20 were cured after one course of penicillin, with total doses of from 800,000 to 2,200,000 units being given in from two to five and one-half days. Lesions recurred in six patients after a course of penicillin lasting two or three days with a dosage of 200,000 units twice a day. Two patients did not return after the second or the third injection. It appears that penicillin therapy should be continued until the lesion desquamates.

Delayed Effects of Ultraviolet Burns.—It has been shown that after exposure to ultraviolet radiation there may be a reduction in sweating-rate, which is partly caused by occlusion of sweat-gland ducts in the necrosed surface layer of the epidermis and probably partly by reduction of secretory pressure of sweat. Thomson reports collapse in two men, apparently attributable to previous ultraviolet radiation, and the development of sun blisters in another case. The two men had been acclimatized by 14 days of exposure to heat, working and resting intermittently according to the same routine for four hours in a climatic chamber. The men collapsed in a heated room a day after receiving ultraviolet burns, one from the sun, and the other from an ultraviolet lamp. They had withstood the environmental conditions (effective temperature 91 F.) on control days without undue hardship. The author says that two kinds of blisters may develop after ultraviolet burn. The more important type arises between the dermis and the epidermis within 48 hours of injury, contains a plasmalike exudate, and should be treated like thermal second-degree burns. The second type (sudamina) arises superficially in the corneum from the second day on after injury, contains sweat, and requires no treatment.

Medical Journal of Australia, Sydney

1:637-672 (May 5) 1951

Some Points in Management of Varicose Veins. C. H. W. Lawes.—p. 637.
•Syndrome of Gout. E. G. McQueen.—p. 644.
•Haemorrhagic Conditions Connected with Thromboplastin Complex, with Particular Reference to Inhibitors. P. Fantl and J. A. McLean.—p. 650.
Penetrating Injuries of Rectum. E. Wilson.—p. 654.
Multiple Myeloma: Review of Literature and of Eight Cases from Royal Melbourne Hospital. D. C. Dowling.—p. 655.
Some Observations on Poliomyelitis Epidemic at Stanthorpe, Queensland, 1951. R. L. Green.—p. 659.

Syndrome of Gout.—McQueen advances the concept of "syndrome of gout," suggesting that the causes of gout are numerous and that the secondary effects of elevated blood uric acid, essential for the syndrome of gout, are manifold. The tendency toward high uric acid level is usually hereditary, the gene determining the condition being an autosomal dominant, which is obscured by endocrine factors in women during the child-bearing period. The mode of action of this hereditary abnormality is still not proved, but circumstantial evidence suggests that it acts through the kidney in diminishing excretion of urates. One important acquired cause of high uric acid level is excess production of uric acid. Diseases of blood may be accompanied by a very high level of uric acid. On numerous occasions gout has been reported in association with erythremia, pernicious anemia, and hemolytic anemia. The other important cause of elevated uric acid level is renal deficiency, which, when sufficiently far-advanced, causes retention of uric acid. Of 65 patients, 58 men and seven women, reported on by the author, 38 are considered to have had renal disease, as shown by urea retention, consistent albuminuria, or albuminuria with urinary deposit of red blood cells and casts. Arteriolar nephrosclerosis is the lesion most consistently recorded in gout. Many resemblances can be seen between the Kimmelstiel-Wilson syndrome and gouty renal disease, and it is suggested that elevated uric acid is a stress-producing agent. The prodrome of an acute attack of gout (increased electrolyte excretion) suggests temporary inadequacy of adrenal cortical secretion, as does the immediate relief of the acute attack by the administration of corticotrophin (ACTH) and cortisone.

Hemorrhagic Conditions Connected with Thromboplastin Complex.—Seven patients, five males between 5 and 15, one woman 44, and one man 75, with hemorrhagic tendencies are reported. Of the five male children, two were hemophiliacs with a positive family history. Hemophilia is defined as a congenital deficiency disease due to lack of a plasma-soluble precursor of thromboplastin. If one assumes this concept to be correct, the laboratory diagnosis of hemophilia can be made by the following three tests: 1. Determination of the whole-blood coagulation time. Delay indicates that the hemorrhagic tendency is due to intravascular causes. 2. Determination of the plasma coagulation time with a series of dilutions of brain extract. This test indicates deficiency in the thromboplastin complex. 3. Determination of the plasma coagulation time with a mixture of patient's and normal plasma. This test indicates whether the condition is due to lack of thromboplastin or is caused by an inhibitor. According to clinical symptoms and results of laboratory tests, two of the young male patients were true hemophiliacs, but there was no family history of bleeding. Other workers have also reported male "bleeders" with a hemophilic defect without a family history of disease. An acquired hemorrhagic condition, occurring in both sexes and simulating hemophilia was found in the authors' two adult patients. The presence of thromboplastin antagonists could be verified. It is known that the patients had acquired the hemorrhagic condition prior to blood transfusion. Iso-immunization against the antihemophilic globulin or against the thromboplastin has been considered. However, antibodies reacting with normal plasma components were not detectable in the patients' plasma. The source of the anticoagulant could not be established.

Medizinische Welt, Stuttgart

20:729-764 (June 2) 1951. **Partial Index**

Vitamin B_{12} in Treatment of Pernicious Anemia. H. Kleinsorge and G. Klumbies.—p. 740.
Nature and Symptomatology of Constitutional Hemolytic Icterus with Elliptopoikilocytosis and Increased Resistance of Erythrocytes. G. Patrassi.—p. 744.
•Inoculation Vaccinia: Treatment with Aureomycin. G. Polemann.—p. 747.
Treatment of Infectious Intestinal Diseases. J. Seiler and C. Gaedeke.—p. 749.

Aureomycin in Inoculation Vaccinia.—A woman, 25, had been subject to eczema since the age of 10. The present disorder began with the appearance of some pustules around the mouth, to which the patient applied boric acid ointment and alcohol. A physician injected calcium and prescribed an ointment, but despite this treatment the skin lesions advanced so rapidly that hospitalization became necessary. Face, neck, and chest were covered with pustules and yellowish crusts, and the face was edematous. So far as the patient knew, she had not been in contact with newly vaccinated children, but the eruption occurred at a time when many children were being revaccinated. This fact, the nature of the cutaneous lesions, and the demonstration of Paschen's inclusion bodies justified the diagnosis of inoculation vaccinia. The cutaneous lesions and fever subsided rapidly with aureomycin therapy.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

95:1665-1728 (June 9) 1951. **Partial Index**

Prognosis in Erythrodermia and in Generalized Dermatoses. J. W. H. Mali.—p. 1675.
•Pulmonary Disorders Caused by Molds. P. J. van der Werff.—p. 1682.
•Treatment of Symptomatic Psychosis with Antallergan (Antihistamine Preparation). F. J. Tolsma.—p. 1690.

Pulmonary Lesions Caused by Molds.—A patient was hospitalized with a diagnosis of asthma and chronic bronchitis. His first severe attack had come on during the harvesting of rye. His general condition remained favorable, but then he declined rapidly. The Pirquet and Mantoux tests were negative, and sputum examination yielded no tubercle bacilli but did reveal Staphylococcus aureus and Neisseria organisms as well as spores of molds. Pulmonary carcinoma was considered. Attempts to

counteract the bronchobacterial factors by a protein preparation of apathogenic bacteria and particularly by penicillin proved ineffective. When further sputum studies suggested the presence of molds and yeasts, treatment with neoarsphenamine was instituted and proved effective. The author gives a detailed description of a second case in which bronchomycosis was associated with cavitation and mentions three other cases of pulmonary lesions caused by molds observed within a short period at an Amsterdam clinic. Potassium iodide, creosote, and especially neoarsphenamine give good results in cases of this type. The clinical picture of diseases generally referred to in the literature as bronchomycosis are in reality pneumonomycoses. The condition may take the form of bronchitis, acute bronchopneumonia, or indurating pneumonia, but, as a rule, it greatly resembles tuberculosis. In cases in which examination of the sputum for bacteria fails to clarify the etiology, molds and yeasts should be searched for. The author comments on the culture and differentiation of fungi.

Antihistamine Preparation in Symptomatic Psychosis.—Assuming that a symptomatic psychosis might be the result of an allergic encephalopathy, Tolsma used the synthetic antihistamine product "antallergan" (N-dimethylaminoethyl-N-benzylaniline hydrochloride) in the treatment of three cases. The usual dose was 80 mg. three times daily. Results were favorable. In the three reported cases the symptomatic psychosis was preceded by influenza, pregnancy, and rheumatic polyarthritis, respectively. One case is discussed to illustrate that symptomatic psychosis may be irreversible.

Presse Médicale, Paris

59:909-932 (June 30) 1951

*Appearance of Pulp of Toes in Patients with Arterial Obliteration: Its Prognostic Value. R. Leriche.—p. 909.
Therapeutic Utilization of a Sulfonamide Compound with Enhanced Solubility. A. Ravina and H. Chimènes.—p. 909.

Appearance of Pulp of Toes in Arterial Obliteration.—It is often difficult to determine whether a patient with arterial obliteration may be benefited by arteriectomy or gangliectomy. The appearance of the pulp of the toes of the patient is of value in establishing a correct prognosis. Arteriography, performed on patients in whom the pulps of the toes were uniformly rose-colored, showed that there was reutilization of the main blood vessels below the thrombosed zone. This reutilization is the essential prerequisite for the nutrition of the tissues. Only the main blood vessels are capable of distributing the blood to all the tissues. On the contrary, ivory white or purple appearance of the pulps of the toes is an unfavorable sign. Although the pulps may occasionally regain their normal appearance after arteriectomy or gangliectomy, there is no certainty that the patient will be benefited by the intervention. Comparative examination of the soles of both feet of the patient may also furnish valuable indications. One completely ivory-white sole and one normal sole may suggest an iliac obliteration. If both soles are ivory-white, obliteration of the aorta or of both iliac arteries should be considered.

Rassegna Medica Sarda, Cagliari

53:1-38 (Jan.-Feb.) 1951

Hyperglycemia Produced by Administration of Uric Acid in Albino Rats on a Diet Deficient in Sulfur. G. Liguori.—p. 1.
*Pneumatosis Cystoides Intestinalis: Clinical Study. E. Capovilla.—p. 7.
Coagulants and Anticoagulants. R. Camba.—p. 23.

Pneumatosis Cystoides Intestinalis.—The occurrence of pneumatosis cystoides intestinalis is reported in two patients, a woman 25 and a man 28, who were admitted to the hospital with pain in the right side of the lower abdomen. Diagnosis of chronic appendicitis was made. When laparotomy was performed, gas-filled cysts were observed in the ileocecal junction and in the ascending colon of the woman and in the omentum and the visceral peritoneum of the other patient. Microscopic examination of the removed appendix of both patients revealed infiltration with neutrophil and eosinophil leukocytes in the parietal layers. Microscopic examination of the removed fragments of the peritoneal serous membrane, in which gas-containing cysts were observed, showed that the cysts had a lining of endothelial tissue and an outer wall of connective tissue, with a few smooth muscle and elastic fibers. Giant cells were not observed. Roentgenologic examination without contrast medium was performed 24 hours after the operation and was negative in both patients. The postoperative course was uneventful. Both patients were in good health two years after the operation. The exact etiology of pneumatosis cystoides intestinalis has not been established. Various theories have been advanced. It is believed that because of atrophy of the intestinal mucosa or a disturbance in its function of absorption an accumulation of gas-producing substances may occur in the lymph vessels of the intestinal wall. Pneumocysts then arise, and, by a process of osmotic equilibrium with the fluids of the organism, the gas comes to resemble air in composition. Diagnosis of the disease is difficult; most of the 200 cases reported in the literature were discovered accidentally in the course of necropsy or, as in the author's cases, during exploration of the abdomen for other disturbances. Pneumatosis cystoides intestinalis is generally associated with other intestinal diseases and does not require specific treatment. Surgical or medical treatment of the associated disorder may simultaneously cause disappearance of symptoms of pneumatosis cystoides intestinalis. Partial removal of the cystic wall is advisable when large subserous gas-containing cysts cause intestinal occlusion. Intestinal resection should be performed only in cases in which occlusion is total and permanent. This may occur especially in cases of submucosal pneumatosis.

Revista Brasileira de Cirurgia, Rio de Janeiro

21:237-320 (April) 1951. **Partial Index**

*Treatment of Rectosigmoid Cancer. S. D'Avila.—p. 251.

Rectosigmoid Cancer.—D'Avila reports on conservation of the sphincter in 50 patients of either sex operated on for rectosigmoid cancer in advanced stage. Anterior resection was done in 26 patients, abdomino-endo-anal proctosigmoidectomy in 17, and posterior resection in two. Five patients died in the postoperative period from diseases not related to cancer. In the group of patients who had anterior resection, special reference is made to 17 patients who had the operation between 1948 and 1950. There were five local recurrences (29.4%). Three patients with recurrences and one with metastasis to the liver died within one or two years from the operation. Thirteen patients (76%), including two with local recurrences, are living, between one month to two years after the operation. In the group of 17 patients who had proctosigmoidectomy, local recurrences occurred in three cases (11.7%). One patient with recurrence and one with metastasis to the liver died within two years after the operation. Fifteen patients, including two with recurrences, are living, from three to seven years after the operation. The two patients who had posterior resection had no local recurrences. They are living, two months and one and a half years after the operation, respectively. The author emphasizes the clinical anatomic, pathological, and social importance of the conservation of the sphincter in patients with rectosigmoid cancer. He concludes that primary resection gives better functional results in cases of rectosigmoid cancer than abdomino-endo-anal proctosigmoidectomy and posterior resection. The survival period of five years after the operation cannot be evaluated, as only four patients in the group lived between five and seven years after the operation.

Semaine des Hôpitaux de Paris

27:1813-1842 (June 6) 1951. **Partial Index**

*Paraaminosalicylic Acid in Treatment of Nonmiliary Pulmonary Tuberculosis: Roentgenoclinical Study. P. Véran and U. Guinot.—p. 1813.
Two Sulfone Compounds Associated with Paraaminosalicylic Acid in Treatment of Pulmonary Tuberculosis. (Roentgenoclinical Study). P. Véran, N. Rist, J. Cottet and U. Guinot.—p. 1820.
*Resistance of Mycobacterium Tuberculosis to Paraaminosalicylic Acid. N. Rist, P. Véran, B. Ballet and others.—p. 1823.

Paraaminosalicylic Acid Therapy in Pulmonary Tuberculosis.—Paraaminosalicylic acid was given to 233 patients with pulmonary tuberculosis for periods varying from 50 days to eight months, with a follow-up period of three to six months. All the patients had a complete rest for several weeks before institution of treatment. Twenty to 25 gm. of the drug (30 gm. for

patients with body weight over 70 kg.) was given in eight divided doses in 24 hours, five days a week for six weeks. Treatment was continued for two to eight months with eight-day interruptions every six weeks for repeated laboratory tests. Treatment was terminated because of intolerance, therapeutic failure, lack of improvement for four to eight weeks, or institution of collapse therapy. In patients in whom the drug is effective, the symptoms subside rapidly within several weeks; if response is slower, continuation of the treatment for two or three months more is not only useless but harmful, since it usually causes clinical and bacteriologic resistance to the drug. The antipyretic effect of the drug and the reduction and clearing of the sputum induced by the drug were pronounced, resulting in functional improvement, which, although only temporary, may be of great importance in certain patients. The authors do not share the opinion of others that patients treated with paraaminosalicylic acid may no longer be considered as bacteriologic carriers. Patients with recent nodular lesions responded best to the drug, while those with cavitary lesions were therapeutic failures. Clear or suppurative effusions associated with intrapleural or extrapleural pneumothorax were not benefited. A favorable effect of the drug was observed in patients with acute serofibrinous pleurisy, particularly with intravenous administration. The drug was best tolerated when administered by intermittent intravenous drip, but roentgenologic improvement was not increased by this route of administration. Although less effective than streptomycin, paraaminosalicylic acid has a definite place in the treatment of pulmonary tuberculosis, because of the bacteriologically satisfactory results from combined treatment with streptomycin or sulfones and because of its favorable effect on fever and sputum.

Resistance of Bacillus Tuberculosis to Paraaminosalicylic Acid.—Forty-three patients with cavitary pulmonary tuberculosis were treated with paraaminosalicylic acid (20-25 gm. daily by mouth) for eight to 36 weeks. The sensitivity of Koch's bacillus to the drug was determined in vitro. Strains to be considered resistant are those yielding visible growth in culture in Dubos medium containing 2.5 γ of paraaminosalicylic acid per cubic centimeter three weeks after the inoculation of 0.01 mg. of bacilli (moist weight) into 5 cc. of medium. Before treatment, 11% of the strains were resistant; after 70 days of treatment 61% were resistant; after 126 days 88%, and after 182 days 100%. Comparison of the curves of resistance of Koch's bacillus to paraaminosalicylic acid in the course of treatment to those of streptomycin resistance in the course of streptomycin therapy showed that the incidence of resistance to paraaminosalicylic acid equaled that to streptomycin. This resistance is responsible for the inefficacy of the treatment. Resistance should be prevented by limiting the duration of treatment with paraaminosalicylic acid alone to four to six weeks and by limiting the indications to noncavitary forms of tuberculosis and to using the drug occasionally for preparatory treatment preceding surgical collapse therapy for cavitary tuberculosis. In those cases in which prolonged streptomycin therapy may be anticipated, it should be combined with paraaminosalicylic acid treatment starting the fifth week at the latest. In those cases in which streptomycin is contraindicated, combined treatment with sulfone compounds and paraaminosalicylic acid should be practiced.

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27:2109-2168 (July 2) 1951

*Direct Epicardial Electrocardiograms (Electrograms) Obtained in Course of Five Surgical Interventions on Human Heart. G. Carouso, H. Chevalier, B. I. Latscha and J. Lenègre.—p. 2109.
Angina Pectoris and Calcific Aortic Stenosis: Twenty Anatomicoclinical Observations. A. Mathivat, D. Lembessis and R. Paulon.—p. 2119.
Coagulability of Blood in Cardiac Decompensation Before and After Treatment. J. L. Beaumont and J. Lenègre.—p. 2128.

Epicardial Electrocardiograms from Human Heart.—In the course of surgical intervention, 27 epicardial electrocardiographic tracings were taken directly from the hearts of five patients. Of these, three with right ventricular hypertrophy were subjected to subclavicular-pulmonary anastomosis for tetralogy of Fallot; one with left ventricular hypertrophy was subjected to resection for coarctation of the aortic isthmus; and one with an almost normal heart to ligation of patent ductus arteriosus. The exploring electrode was connected with the wire of the unipolar precordial leads, and the indifferent electrode was connected with the central terminal of Wilson, as for unipolar precordial recordings. The sterilized exploring electrode was inserted through a buttonhole incision of the pericardium, 3 to 5 cm. in length, and was brought into immediate contact with various areas of the epicardial surface, without interposition of cotton. This was done without causing any immediate or late untoward reactions. The conclusions drawn from the direct tracings were as follows: 1. In patients with right ventricular hypertrophy, various types of R, RS, Rs, and rS were observed, according to the explored areas of the right ventricle, and types of qRS and QRS complex were obtained with the electrode exploring the left ventricular epicardium. When the electrode is placed on the right ventricle, the major deflections of the R wave express well the variations of the potential of the right ventricular epicardial surface, particularly in the dense area of the right border and of the supraventricular ridge. When the electrode is placed on the left ventricle, the major deflections of the S wave accurately show the variations of the potential of the hypertrophied right ventricle. The types rS or RS of the hypertrophied right ventricles manifest variations of the potential of certain zones of the epicardial surface of the right ventricle, such as the trabecular zone and the anterior surface between the trabecular zone and the infundibulum pulmonis. 2. In the patient with left ventricular hypertrophy the direct leads revealed tracings of rS and RS types at all the areas of the right ventricular epicardium and of qR type at the left ventricular epicardium. 3. The direct electrocardiographic tracings obtained from patients with right or with left ventricular hypertrophy resembled closely the tracings obtained by the unipolar precordial method; this shows the high diagnostic value of Wilson and co-workers' unipolar precordial recordings. 4. The tracings obtained with direct epicardial leads revealed that even in true right ventricular hypertrophy the left epicardial surface (left border and posterior aspect of the left ventricle) shows an initial electronegativity. This observation proves that the first cardiac vector moves from the left to the right, even in the presence of great changes in the weight relationship between the two ventricular masses (right ventricular hypertrophy).

Strahlentherapie, Munich

85:205-352 (No. 2) 1951. Partial Index

Histological Investigations on Immediate Reaction of Cell Nucleus of Walker Carcinoma of Rat Following Application of Ultrasound Waves. K. Woeber.—p. 207.
Changes in Cell Nuclei Following Application of Ultrasonic Waves. G. Asche.—p. 215.
Influence of Ultrasonics on Wassermann Reaction of Serums from Syphilitic Patients. K. Woeber, J. Zinzius and G. von Wenzlawowicz. —p. 226.
Histological Examination of Excised Carcinomas After Preoperative Roentgen Irradiation. H. G. Stoll.—p. 310.
*Histological Type and Response to Irradiation in Cancinoma of Uterine Cervix. E. Schüller.—p. 321.

Histological Type in Carcinoma of Uterine Cervix.—Schüller analyzed the records of 1,160 women with carcinoma of the uterine cervix who had been treated by irradiation. In only 733 was the histological material adequate for complete analysis. For estimation of sensitivity to irradiation, Pendl's histological classification of cervical carcinomas is superior to Glücksmann's, which leaves too much to subjective interpretation, giving too much attention to the gross pathologic aspects and not enough to the detailed histological structure. Pendl's classification divides the tumors into various types that show a characteristic response to irradiation. The cases reviewed here corroborated Pendl's claim that the predominance of spindle-shaped cells in the mucosal type and the slightly differentiated carcinomas of the parvicellular and macrocellular intermediary type were the ones that responded best to irradiation. The incidence of the different histological types in the cases reviewed here corresponded largely with figures given by Pendl. The histological type of a cancer of the uterine cervix not only permits an estimate of its responsiveness to irradiation but can also aid in the decision as to whether surgical treatment is advisable. Cylindrical cell cancers and certain mucosal types of cancers are not responsive to irradiation, and radical surgical treatment is therefore advisable in these types. Carcinomas surrounded by eosinophilic infiltrations seem to have a good prognosis as regards response to irradiation.

BOOK REVIEWS

The Neuroses: Diagnosis and Management of Functional Disorders and Minor Psychoses. By Walter C. Alvarez, M.D. Cloth. $10. Pp. 667. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1951.

Dr. Alvarez has attempted to bring before the medical profession 45 years of experiences in treatment of disturbed patients. Some of the problems could be understood by a study of the disease, but many of them could be understood only by the study of the persons who had them. In an era when persons are conscious of disease, Dr. Alvarez has attempted to improve the physician's approach to the person who has become the patient.

His approach, as synthesized in 600 pages gleaned from a vast and varied experience in internal medicine, is fundamentally intuitive and empiric. It is based on a common sense evaluation by a sympathetic physician-counsellor who is cognizant of his patient's hopes and aspirations, fears, frustrations, and obligations, as well as his physical make-up and his hereditary endowments.

Dr. Alvarez tends to place much more emphasis on heredity than on environment. The role of each factor is open to a great deal of debate at the present time. His approach is based on experience with a given problem in a given patient rather than on a dynamic psychiatric evaluation of the individual case, as one would be led to believe by the title of the book. Even though Dr. Alvarez attempts to describe and catalogue certain criteria in the neuroses and psychoses, he succeeds more in documenting his personal experience in a vast number of instances, in which he reasons from a particular case to the general principle in drawing his conclusions. While this experience makes interesting reading and may be helpful in a general way to both practitioner and internist, it may be difficult to convey effectively to the reader an approach that is so intuitive. No well-defined concept of the neuroses is presented from either an etiological or a diagnostic point of view.

However, Dr. Alvarez does succeed in offering something of the essence of the manner in which an astute, practical, and sympathetic clinical mind is able to handle the neurotic disturbed patient at the level of the nonpsychiatrist.

Chronic Ulcerative Colitis (Thrombo-Ulcerative Colitis). By J. Arnold Bargen, M.D. Publication number 101, American Lecture Series, monograph in American Lectures on Abdominal Viscera, edited by Lester R. Dragstedt, M.D., Chairman, Department of Surgery, University of Chicago School of Medicine, Chicago. Cloth. $2. Pp. 62, with 3 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto TB, 1951.

Probably no other living physician—or even any physician in the future—can have the experience that Dr. Bargen has had with ulcerative colitis. This short monograph gives a critical review of his clinical experience. He has discussed adequately the diagnosis, with all its ramifications, and the complications that might ensue. The treatment has the usual method outlined for any abdominal disease that is as disabling as ulcerative colitis. Diet is an important factor. Curiously enough, however, Dr. Bargen does not rely so much on vaccine therapy now as he did in the past, and he puts special emphasis on the use of sulfonamides. His experience with antibiotics is comparable to that of others with fewer patients, but he has come to the same general conclusion as to their therapeutic value. The author recognizes that there is some value in parasympatholytic drugs and also in barbiturates.

From a surgical point of view he recommends that ileostomy precede a colectomy. Certainly no one can disagree that in a patient with a long-standing chronic, irreversible disease, ileostomy should precede colectomy and that colectomy should be the operation of choice, as he suggests. Finally, in discussing treatment, Dr. Bargen does give some lip service to the psychosomatic relationships and discusses the time-honored approach of the average physician to psychosomatic aspects of this disease.

At the outset, on page 5 of the introduction, he says. "Anxiety and emotional upsets do not cause ulcerative colitis, but its progression and failure to respond to treatment may well be aided and abetted by an unhappy frame of mind. The mental state of the patient should be observed and psychosomatic relationship to the disease should be discussed in a guarded manner." This use of the words "in a guarded manner" is questionable. Should not the patient become acquainted with the fact that there might be psychological reasons and emotional factors that might be intimately connected with his disease? Should not a patient be taken into a physician's confidence and be told of the etiological and life situations that might interfere with the normal progress and healing in any disease?

Despite these controversial points of view, this monograph will serve excellently for the clinicopathological diagnostic approach to what Dr. Bargen calls "thrombo-ulcerative colitis." He outlines the more or less standard medical management, even including the rather temporary results with corticotropin (ACTH). To those unacquainted with the clinical picture of this disease, organic information elicited should prove of distinct help and edification.

Introduction to a Psychoanalytic Psychiatry. By Paul Schilder, M.D., Ph.D. Authorized translation by Bernard Glueck, M.D. Cloth. $3.25. Pp. 178. International Universities Press, Inc., 227 W. 13th St., New York 11, 1951.

This book is a translation from the original in German, stimulated by the translator's belief that the book represents the first attempt at a systematic presentation of clinical psychiatry on a psychoanalytic basis. Schilder's agreement with Freudian opinion on the clinical symptom-complexes of psychiatry is illustrated in the contention that symptom-complexes ordinarily embrace three types of phenomenon: those representing remains of a normal state or of neurosis, phenomena of a residual nature; those representing the detachment of the libido from its object, phenomena of regression; and those representing attempts at recovery.

The opinion is expressed that psychoanalytic psychology has furnished psychiatry with the possibility of eliminating artificial lines between neuroses and psychoses and between neuroses and so-called normal psychological manifestations. It thereby makes possible the extension of the understanding of psychoanalytic psychiatry to general problems of human conduct that lie outside the strict field of clinical psychiatry.

The book describes in detail the concepts of ego ideal, ego instincts, and phenomena of hypochondriasis, depersonalization, repression, and narcissism. Other chapters consider the basic factors underlying the major psychoses.

Modern Trends in Paediatrics. Edited by Sir Leonard Parsons, M.D., F.R.S., F.R.C.P. Cloth. $12. Pp. 601, with 110 illustrations. Paul B. Hoeber, Inc. (Medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1951.

This is a collection of articles written by contributors who are known for their excellence in the fields they discuss. In no sense has the editor attempted to survey the entire subject of pediatrics. He has selected topics on the basis of recent advances or of present interest in the field. The chapter topics vary from a discussion of preventive pediatric services: recent trends in the United Kingdom, to hemolytic disease of the newborn. Some of the chapters present new information, and some contain better known information in a well-organized manner. Owing to the necessary brevity of the articles, several contributors discuss in chronological fashion the findings and publications that have marked progress. The bibliographies accompanying these chapters are excellent.

Because of the composition of the book and the limited number of subjects that are presented in detail, it is not a general reference or textbook. It would be of greatest interest to the persons with pediatric training who might wish to read articles that concisely summarize the available information on various trends in pediatrics.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

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Spezielle Pathologie der Krankheiten des zentralen und peripheren Nervensystems. Von Dr. Gerd Peters, Professor der Neurologie und Psychiatrie an der Universität Bonn. Cloth. 56 marks. Pp. 437, with 214 illustrations. Georg Thieme, Diemershaldenstrasse 47, (14a) Stuttgart O; agents for U. S. A.: Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1951.

In this book, dedicated to Spielmeyer, the specific pathology of the diseases of the central and peripheral nervous systems is discussed in a well-organized fashion and documented by well-chosen and well-reproduced illustrations, most of them photomicrographs. An attempt is made to correlate anatomic with functional alterations and, not very extensively, with the clinical picture. In addition to inflammatory, circulatory, degenerative, traumatic, and tumorous lesions and malformations, the effects of chemical and physical agents are extensively discussed. This is followed by an unusually useful compilation of the anatomic alterations of the nervous system in the various internal medical diseases, and, finally, by a discussion of the hypothalamic-pituitary syndrome. A large amount of information is compressed into a relatively limited space, and the style is clear. A small number of references are given as footnotes. Almost all the information given can be found in comparable books in English; nevertheless, the unusual completeness of some of the chapters may make the study of this book valuable to the American internist, pediatrician, and pathologist looking for information in neuropathology.

Tuberculosis in the Aged. By Erik Tengve, Med. Lic., Sthlm. [Thesis, M.D., Uppsala University.] Translated by Klas Magnus Lindskog. Paper. Pp. 114, with 3 illustrations. Oriel Blombergs Nya Aktiebolag, Lindesberg, 1951.

In this monograph Tengve reviews the literature on tuberculosis in the aged. He discusses symptomatology and classification of types, and the incidence of tuberculosis in Sweden in several age groups, including that of the aged. The drop in the tuberculosis mortality rate in Sweden, chiefly in the age group 20 to 30, accentuates the mortality rate in the age group over 60. Tuberculosis in old persons has thus acquired a mounting importance. The author suggests also that the relatively high incidence in the aged may be a relic from the times when the tuberculosis mortality rate in Sweden was much higher than it is now and that these facts might justify the assertion that in 10 or 20 years' time we will witness a significant diminution of the general death rate in tuberculosis.

Analysis of cases shows that the percentage of open cases is much higher in old persons with tuberculosis than in other tuberculous persons. It was found, however, that most of the older patients with tuberculosis had had the disease more than a year before they were admitted to the hospital. These persons, who in most cases had chronic and open tuberculosis, must have constituted a source of infection, especially for their families. It was demonstrated that about one-third of all the children and grandchildren in the families of affected persons as a rule had or had had manifest tuberculosis of the lungs. It was also shown that about one-fourth of all the cases were known to the dispensaries before the patient's admission to the hospital. This extremely careful and well-reasoned summary has a significant application to the problem of control of tuberculosis in this country.

Das Elektrokardiogramm: Theorie und Klinik. Von Dr.med. Hans Schaefer, o. Professor und Direktor des physiologischen Instituts der Universität Heidelberg. Cloth. 55 marks. Pp. 556, with 349 illustrations. Springer-Verlag, Reichpietschufer 20, Berlin W. 35 (West-Berlin); Neuenheimer Landstrasse 24, Heidelberg; Göttingen, 1951.

This extensive monograph on the electrocardiogram represents a significant contribution to the subject. The monograph's strength lies in its handling of theory. The clinical aspects are less satisfactory, and the section on arrhythmias is not so outstanding. The author has taken the opportunity in this monograph to expand the important contributions made by himself and his co-workers to the theory of electrocardiography.

The first section deals with the theory of action potentials; the second, with its application to the actual recording of cardiac events. Use is made of the monophasic curve, of current flow inside and outside the muscle cell, of the depolarization and repolarization processes, and of vector analysis. Also considered is the concept of solid conductors. The remaining sections deal in turn with the QRS complex, the S-T and T complexes, and the arrhythmias. The monograph closes with a consideration of chest leads.

A mass of data are presented in this tome. It is lengthy and repetitious at times, as would be expected from the traditional German style of presentation. It embodies some extremely stimulating ideas, which do not always parallel teachings current in this country. For example, the concept, recently advocated by Robb, that the conduction system stimulates the heart muscle segmentally, making it, as it were, a series of islands "innervated" by the conduction system, carries with it a great many possibilities. In considering the T wave, the author points out that, in addition to the contour determined by the ventricular gradient, which has a vector opposite in direction to that of QRS, T contour is influenced by another vector directed from base to apex, determined by a "metabolic gradient"; and, in the case of injury, by a third vector oriented in a direction opposite to the vector depicting the injury S-T deviation.

The author makes use of vector analysis in the frontal plane based on the Einthoven triangle concept. As a matter of fact, except for the more or less isolated sections at the end dealing with precordial leads, the discussion is concerned primarily with the frontal plane. The author points out that the unipolar lead connection, even when the electrode is on the heart itself, has so much extrinsic distortion in it that the use of the R wave peak in such leads to determine the onset of the intrinsic deflection is fraught with error. He favors, generally, the dipole field theory, in which all regions of the heart have somewhat equal influence on the electrocardiogram. Actually, each region has an influence varying with the square of the distance from the electrode and directly with its thickness and area. There are some elaborate mathematical developments, particularly in regard to precordial leads. In employing mathematical formulation and vectors, the author points out that they are only approximations of the actualities, owing among other things to the fact that the field surrounding the heart is not homogeneous.

This monograph is highly recommended to the serious student of electrocardiography. It is not suitable for the beginner or casual reader. The stimulation, the new ideas, and the reorientation toward some of our "traditional," though recently developed, views on electrocardiography will more than compensate anyone for the energy employed in unravelling the details. Merely a study of the theoretical presentation by means of the diagrams will be extremely illuminating.

DeLee's Obstetrics for Nurses. By M. Edward Davis, M.D., Joseph Bolivar DeLee Professor of Obstetrics and Gynecology, University of Chicago, and Catherine E. Sheckler, R.N., M.A., Assistant Professor of Nursing Education, University of Chicago, Chicago. Fifteenth edition. Cloth. $4.50. Pp. 673, with 387 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1951.

This is a well-organized, well-integrated, and beautifully written textbook of obstetrics for nurses. Eminent in their own fields, the authors have recognized essential facts and procedures for nurses, presenting them in concise form with an added pleasant readableness. Obstetrics and obstetric nursing is a vast field with ever-broadening horizons. The quality of this book is greatly enhanced by the artful presentation of recent advances in the immediate and allied spheres by contributing authors proficient and practiced in their subjects.

Particularly gratifying are the chapters on community aspects of maternal and infant care, home nursing, and the emotional aspects of pregnancy. The nurse's role is a signal one in the area of prenatal care, the greatest contributing factor in the reduction of maternal and infant morbidity and mortality rates. The marked advances in these phases engender interest and competence in the nurse, and, therefore, serenity and confidence in the patient and her family.

Figures and statistics are accurate and compare with those cited from other large surveys in recent literature. Illustrations are excellent and completely up-to-date, many being photographs taken in the authors' clinical field. The authors have retained the unit format of previous editions and have succeeded in adequate revision plus recent bibliographies. A fine sense of human devotion, a true philosophy of medicine pervades the book.

The Collected Papers of Adolf Meyer. General Editor: Eunice E. Winters. Volume I: Neurology. With Introduction by Louis Hausman, M.D., Professor of Clinical Medicine (Neurology), Cornell University Medical College, New York. Volume II: Psychiatry. With introduction by Sir David K. Henderson, M.D., F.R.C.P., Professor of Psychiatry, University of Edinburgh, Edinburgh. Cloth. $30, per set of 4 volumes. Pp. 693, with illustrations; 674 with portrait. Johns Hopkins Press, Homewood, Baltimore 18, 1950; 1951.

Adolf Meyer was the proponent of important psychiatric theories and a physician of diverse interests, among which can be listed medical education. It is extremely unusual that a man of these qualifications should not have written a book. Instead of this, Dr. Meyer during his lifetime had the occasion to publish more than 250 papers in many European and American journals. The books he did not publish have been published for him in the form of his collected papers. This set will comprise four volumes. Volume 1 is devoted to Meyer's neuroanatomic, neurological, and neuropathological papers. Review of these papers makes abundantly clear his wide range of interests and his keen perception of basic principles. His work on the optic radiation, a portion of which bears his name (Meyer's loop) is a model of correlation of evidence from several disciplines. The neuroanatomy of the optic radiation was worked out with great care. The evidence from pathological lesions was brought to bear on the anatomic principles, and then both the anatomy and pathology were given clinical application. Though some of the theories that Dr. Meyer propounded on the functioning of the nervous system are probably outdated, his observations are always worth reading and at times are a model of description.

It is fitting that the volume on psychiatry (Volume 2) should follow the one on neurology. This is both chronologically and developmentally correct in the reconstruction of Dr. Meyer's interest in medicine. He made no great secret of the fact that his psychiatric concepts had proceeded from his interests in the basic neurological sciences, and expressed this in calling his approach psychobiological. In view of the recent emphasis of psychoanalytical principles in psychiatry it may seem almost archaic to contemplate some of the Meyerian theories. However, a review of his papers in psychiatry is provocative on many points, two of which may be mentioned. First, it is amazing how many of Dr. Meyer's concepts now seem commonplace. This, however, is only because they are taken for granted, and their universal applicability only adds to Dr. Meyer's fame in originally propounding them. Secondly, it is refreshing to read some of his appraisals of psychoanalytical theories. It seemed a characteristic facet of his greatness to be able to give just due to men and to theories that might be considered opposed to his. In these days when discussion between various psychiatric schools brings more heat than light, Meyer's inherent fairness seems like a world apart.

The two volumes in many ways are complementary to each other. The purpose of the editor was to present Meyer's views of psychiatry and neurology as he expressed them through his papers. In some sections of the volumes one wishes that critical correlation and evaluation had been attempted. This, however, was not the editor's purpose. Her intentions were to let Adolf Meyer speak for himself. This he does in a lucid and instructive manner.

Problems of Consciousness: Transactions of the First Conference, March 20-21, 1950, New York, N. Y. Edited by Harold A. Abramson, M.D. Cloth. $3. Pp. 200, with 15 illustrations. Josiah Macy, Jr. Foundation, 565 Park Ave., New York 21, 1951.

This is a verbatim report. Participants in the conference were 18 outstanding scientists from the fields of psychology, psychiatry, physiology, biology, embryology, and zoology. Discussion material is presented on an informal basis and centers around the problem of sleep-wakefulness cycle, psychoanalytic concepts of sleep and dreams, perception of pain, phenomena of hypnosis, and consciousness and the chemistry of time.

The major purpose of the conference was to attempt to overcome the difficulties in communication, both emotional and semantic, between the many disciplines involved in the discussions and thus, through mutual understanding, to move toward a unification of interpretation in all fields of science, so that a "science of man" might be developed in which medicine is considered to play a central role.

Surgical Pathology of the Mouth. By E. Wilfred Fish, C.B.E., M.D., Ch.B., Dental Surgeon St. Mary's Hospital, London. Cloth. $10. Pp. 463, with 236 illustrations. J. B. Lippincott Company, 227-231 S. 6th St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1951.

The author has written this textbook for the dental student or the practitioner as representing the irreducible minimum of pathology necessary for an understanding of daily practice and for prediction of results. The book is not intended to replace or even approach the content of a textbook on general pathology. Each chapter closes with a summary that is largely a restatement of the material content rather than an epitome of prevailing opinion. Some of the subjects treated are as follows: cell growth and degeneration; repair of the calcified matrix; circulatory disturbances; inflammation; chemotherapy and bacterial defence; surgical pathology of bone; pathology of dentine and dental pulp, of the cementum, of the pulpless tooth, of the mucosa, of the parodontal tissues, and of the enamel; foci of infection, neoplasia; mesenchyme tissue tumors; epithelial tumors and tumors arising from specialized tissue; and tumors of developmental origin.

The author presents his material in a lucid style. The format and type are good, as are the photomicrographs and other illustrations. The author writes on the basis of a broad experience in dental practice and general information. There is little bibliography. It is difficult to determine the position of this textbook among others in medical sciences, because the title could imply a specialized treatment of the diseases of the mouth region, when actually the author states that the purpose of his book is to give the student and practitioner the minimum pathology essential to intelligent practice. The title accordingly can be disadvantageous, because students and practitioners of dentistry will not realize that the book has much valuable information for them, and surgical pathologists will be disappointed in finding that this is not a book on special pathology of the mouth.

Good Health for You and Your Family. E. Patricia Hagman, Ed.D., Editor, Associate Professor of Health and Physical Education, Teachers College, Columbia University, New York. Prepared from publications of Health and Welfare Division, Metropolitan Life Insurance Company. Cloth. $3.75. Pp. 305, with illustrations. A. S. Barnes & Company, 101 5th Ave., New York 3, 1951.

As would be expected, because this volume presents material assembled from health and welfare publications of the Metropolitan Life Insurance Co., sensible recommendations and reliable information are provided. The editor has set up the data in four sections, with some slight overlapping. The first section contains hints for good health, with chief emphasis upon food and nutrition, and has numerous helpful charts and other illustrations on this subject.

In the second section, dealing with common diseases and disorders, 32 conditions are given detailed attention, ranging from appendicitis to whooping cough. Discussions of many of these were prepared with the assistance of interested national voluntary or governmental agencies. The third section, on child care, includes information for expectant mothers, tabulations on common childhood diseases, an immunization timetable, measurement of physical growth, consideration of behavior problems, and discussion of child safety. The final section, on safety and first aid, is especially well done and complete. There are detailed recommendations regarding accident prevention both in the home and elsewhere, and well-illustrated directions regarding first aid procedures. Physicians can recommend this book to their patients without reservation.

Handbook of Psychology. By John H. Ewen, F.R.C.P.E., D.P.M. Cloth. 25s. Pp. 215. Sylviro Publications, Ltd., 19 Welbeck St., London W.1, 1950.

This handbook is intended for students who are taking up the study of psychology for the first time. The author has attempted to describe the essential principles involved in psychology and the practical implications of these principles in practice. The relationships of so-called normal psychology to psychologic medicine are described. Short chapters on methods of treatment in psychoanalysis and other psychiatric and physical treatments of mental disorder are included.

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Emotional Factors in Cardiovascular Disease. By Edward Weiss, M.D., Professor of Clinical Medicine, Temple University School of Medicine, Philadelphia, Penn. Publication number 97, American Lecture Series, monograph in American Lectures in Circulation, edited by Irvine H. Page, M.D., and A. C. Corcoran, M.D. Cloth. $2.25. Pp. 84. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1951.

This is a well written book in nontechnical, popular style. No phase of the subject is gone into deeply, because this book is written for the practicing physician and not for the psychiatrist. A few sentences in the introduction are worth quoting: "The traditional old family doctor very often was an excellent psychosomatic physician, although he never thought of himself as such. His patients usually were intimate friends, and he was as familiar with their emotional life as with their physical peculiarities. He was well aware that the two frequently were closely related." The present-day complexities of medical practice have taken the physician away from this intimate contact with his patient. However, the emotional factors are still present and need evaluation in respect to diagnosis and treatment. That is precisely what the author has done in this book.

The problems of "cardiac neurosis," functional heart disease, neurocirculatory asthenia, hypertension, the cardiac with superimposed anxiety, and psychosis in cardiac disease are discussed clearly and concisely and are illustrated by well-chosen case reports. This book is an excellent companion volume for the others that have appeared in the series of American Lectures in Circulation.

Micro-Analysis in Medical Biochemistry. By E. J. King, M.A., Ph.D., D.Sc., Professor of Chemical Pathology in University of London (Postgraduate Medical School), London. Second edition. Cloth. $3.50. Pp. 222, with 22 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1951.

This textbook of clinical chemistry contains clear, concise directions for determining the functioning of various organs and for analyzing small amounts of body fluids, feces and urine, calculi, and gastric and duodenal contents. Besides giving instructions for specific tests, the author discusses normal values for the methods included in the text, spectroscopic procedures, hydrogen ion concentration, preparation of volumetric solutions, and the use of colorimetric and photometric instruments. Only brief statements are made on the significance of the tests. The organization of the material, the index, and the make-up are good, but it is a little surprising to find directions for determining pH only by means of indicators.

Evolution Emerging: A Survey of Changing Patterns from Primeval Life to Man. By William King Gregory. Collaborative work of American Museum of Natural History and Columbia University. Volume I: Text. Volume II: Illustrations. Cloth. $20, per set. Pp. 736; 1013. The Macmillan Company, 60 Fifth Ave., New York 11, 1951.

This encyclopedic work presents a broad survey of the animal kingdom, with emphasis on the extensive series of evolutionary transformations that have led from ameba to man. The first volume contains 559 two-column pages of text and 144 pages of bibliography. The second volume contains 1,013 pages of illustrations, most of which are clearly labeled line cuts. In many instances, the drawings represent series of animals or of structures arranged along comparative-systematic lines to indicate the range and evolution of form in a given group. The book presents a stimulating review of the evolutionary concept in an easy, informal style.

The Chemistry and Technology of Food and Food Products. Prepared by group of specialists under editorship of Morris B. Jacobs, Ph.D., Adjunct Professor of Chemical Engineering, Polytechnic Institute of Brooklyn, Brooklyn. In 3 volumes. Volume I. Second edition. Cloth. $12. Pp. 832, with illustrations. Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 2a Southampton Row, London, W.C.1, 1951.

The first edition of this comprehensive work consisted of two volumes, but, because of the great progress made in food technology and chemistry since its appearance in 1944, the current edition has had to be expanded to three volumes. These present a complete description of the technical aspects of foods, their sources, composition, processing, and the related body physiology. Because of the great difficulty any one person would have in surveying adequately the entire field of food chemistry and food technology, 39 authors, each a specialist in his field, have contributed to this authoritative work. Among them are food technologists, chemists, chemical engineers, biochemists, bacteriologists, sanitary engineers, public health officers, food inspectors, and entomologists. Several contributors to the first edition were not able to revise their chapters on time, and the editor, who is well-versed in the broad subject of food control, has done an excellent job of revising the chapters concerned.

The first part of Volume 1 deals with fundamental food chemistry and contains an extensive discussion of the known nutrients, and their chemistry and function in the body. It is noted that no mention is made of the use of iodized salt as a dietary source of iodine. Also the statement is made that vitamin D_3 is about 1.5 times more efficient in man than vitamin D_2. The Council on Foods and Nutrition of the American Medical Association does not recognize any difference between vitamins D_2 and D_3 in man. The use of the term "vitagens" referring to a group of so-called essential food fractions is not in general usage and may be new to many readers.

Part 2 discusses unit operations and processes that apply to most foods, such as evaporation, extraction, mixing, and dehydration. Part 3 is concerned with the maintenance of sanitary and quality control. Stress is given to the proper use of pesticides in preventing contamination of foods. In spite of the fact that this edition is advertised as completely revised the Council on Foods and Nutrition is still incorrectly referred to on page 612 as the Committee on Foods, a name that went out of use in 1936.

Throughout the entire volume there are frequent references to the literature, and a bibliography is included at the end of each chapter. This volume is a combination textbook on food chemistry and source of general information on food processing. It is aimed at the food technologist, but the physician and graduate student interested in foods will find it a profitable addition to his reference library.

Hospital Staff and Office Manual. By T. M. Larkowski, M.D., F.A.C.S., Professor of Clinical Surgery, Stritch School of Medicine, Loyola University, Chicago, and A. R. Rosanova, R.Ph., M.D., Clinical Instructor, University of Illinois Medical School, Chicago. Cloth. Pp. 428, with illustrations. Romaine Pierson Publishers, Inc., 676 Northern Blvd., Great Neck, New York, 1951.

If one has ever had the experience of being a naive substitute intern tossed into the maw of a busy medical ward and confronted with terrifying orders to perform hypodermoclyses, spinal taps, and bewildering laboratory procedures, he will regret that this valuable little manual was previously unavailable.

Tersely restricted to essentials and amply illustrated, it scans routine hospital techniques, laboratory procedures, electrocardiography, and radiography. It also outlines the specialized examination of the various anatomic systems. It can be recommended as an excellent handbook for the senior medical student, intern, and practitioner as a reminder of the essentials of medical practice.

Primer on Alcoholism: How People Drink, How to Recognize Alcoholics, and What to Do about Them. By Marty Mann. Cloth. $2. Pp. 216. Rinehart & Co., Inc., 232 Madison Ave., New York 16, 1950.

The author, executive director of the National Committee on Alcoholism, describes causes of alcoholism from a practical, experienced lay viewpoint. He defines the alcoholic drinker as opposed to the "social" or "heavy" drinker and discusses steps to be taken by the family and friends of the alcoholic in their attempts to bring him to effective treatment. Comment is made on methods of treatment through psychiatry, various types of medication, aversion treatment, and effectiveness of Alcoholics Anonymous.

The book is for the laity and is stated to be primarily directed toward the estimated 20 million or more persons who may be in some way related to, or involved with, an alcoholic. The stated object is to provide these persons with the up-to-date basic knowledge and practical information that is available for the proper handling of this disease. The material is well presented, and the chapters concerning psychiatric treatment and the methods of the Alcoholics Anonymous group are of value.

QUERIES AND MINOR NOTES

ENTERITIS IN TOURISTS

To the Editor:—*Many American tourists in Mexico have enteritis (usually mild) soon after arrival. As a rule the general well-being and the appetite are not disturbed; however, some patients have a great number of stools without tenesmus daily. What is the cause of this disease, and what is the best way of treating it?* *M.D., Wisconsin.*

This inquiry was referred to two authorities, whose respective replies follow.—Ed.

Answer.—Many factors may be involved in the enteritis occurring among tourists from the United States in Mexico. Ordinarily the cause is associated with staphylococcic or streptococcic contamination of food, with resulting production of chemical toxins which are highly irritating to the the intestinal mucosa. The extent of the reaction seems to depend on the physical condition of the person involved, being more serious in fatigued individuals. If the diarrhea continues, bacillary infection or amebiasis may be suspected. The diagnosis in these instances can be established only by repeated stool examination. Salmonella infection may also occur.

Symptomatic treatment with milk of bismuth and paregoric is usually satisfactory. Tea should be drunk frequently during recovery in order to restore fluid loss and reduce local irritation. If amebiasis occurs, specific therapy with carbarsone or iodochlorhydroxyquin is usually effective. In bacillary involvement, an intestinal antiseptic such as phthalylsulfathiazole or neomycin is indicated.

Enteritis may be avoided by restriction of fluids to bottled beverages and by avoidance of fresh vegetables or fruits. Salad dressings, ice creams, pastries, and other foods that may be contaminated in handling should be avoided. Except at first-class hotels, tourists would be wise to eat only freshly and well cooked foods.

Answer.—The condition described is extremely common; it is sometimes called "tourist's disease" or "Aztec disease." Actually there are probably several types of acute gastroenteritis that commonly afflict tourists and even natives in Mexico. Some of them are almost undoubtedly due to Staphylococcus or Staphylococcus toxins; others are probably caused by Salmonella or other members of the paratyphoid group. It is important that the mild and temporary gastroenteritis not be confused with more serious infections which are also common in Mexico. Good results are often obtained with streptomycin (1 gm. in 20 cc. of salt solution, taken 10 or 15 drops at a time every hour). Sulfadiazine and either paregoric or some other opium derivative with bismuth have been found effective. If the condition does not clear up in 48 hours with one of the appropriate treatments, it is wise to be examined for other conditions, particularly amebic dysentery or one of the paratyphoids. Actually the severity of the gastroenteritis varies widely, presumably because of differences in the number of germs or amount of toxin ingested and, possibly, individual resistance.

ALLERGIC BLOOD DONORS

To the Editor:—*Should a person who is allergic donate blood for transfusion? Will the recipient become allergic?*

M.D., New York.

Answer.—It is difficult to give a precise answer to this inquiry without more information on the nature of the allergy present. Severe or active allergic manifestations should certainly disqualify a donor, but apart from this a donor may be accepted. The allergic reaction occurs in less than 1% of blood transfusion recipients and appears usually as transient, small urticarial lesions but occasionally as so-called giant edema and rarely as respiratory difficulty attributed to edema of the larynx or asthmatic reaction. Injections of epinephrine usually afford prompt relief. In most instances, questioning of both donor and recipient reveals no history of allergic episodes apart from the transient reaction itself. Systematic efforts to exclude allergic donors have certainly not eliminated this type of reaction. In a few scattered cases, correlation has been observed with specific sensitization of the donor and the recipient has appeared sensitized for up to three months, although it does not appear that such passive sensitization has been associated with any great harm to the recipient.

CHRONIC LEG ULCER

To the Editor:—*A man aged 62 has an ulcer 2½ in. (6 cm.) in diameter just above the external malleolus of the right leg. He does not remember injuring the leg. It began as a small ulcer and gradually increased in size. He was treated with medicated (contura*) bandages for three months with little improvement. His veins are not large and except for the area immediately surrounding the ulcer the skin is in good condition. There is no discoloration or edema. General physical examination discloses no abnormalities. His blood pressure is normal; the Kahn reaction of the blood is negative, and results of urinalysis were negative for albumin, sugar casts, pus and blood. What treatment would you advise? Would ligation and injection of the saphenous vein help the ulcer on the lateral surface of the leg?* *M.D., West Virginia.*

Answer.—Chronic leg ulcer above the lateral malleolus in a 62 year old man in the absence of visible or palpable varicosities or edema may be due to arterial or arteriolar sclerosis (even with a normal blood pressure) or to a broken down granuloma (syphilis, tuberculosis or other granulomatous infection) but most frequently to a low grade skin infection, initially neglected and not bandaged. Complete bed rest in a hospital should be prescribed, with attempts to culture the organism. If no specific cause can be found a wide excision of the ulcer, followed by a split-thickness skin graft is in order, provided arterial circulation is satisfactory. Division of the saphenous vein is not indicated unless valvular incompetence is demonstrated. It would have to be the short saphenous vein, judging from the location of the ulcer.

FIBROUS DYSPLASIA

To the Editor:—*A boy 4½ years of age has polyostotic fibrous dysplasia. The involvement is extensive, with lesions present in the long bones of the upper extremity, pelvis, and lower extremity—all on the left side. The case is further complicated by a pathological fracture through the neck of the left femur, which is healing under immobilization in plaster. May I ask your opinion as to a therapeutic trial of either cortisone or ACTH? Has either of these been used in fibrous dysplasia?*

Richard J. Rushmore, M.D., Florham Park, N. J.

Answer.—The use of the cortisone or pituitary adrenocorticotropic hormone (ACTH) has not been tried in the treatment of fibrous dysplasia (polyostotic fibrous dysplasia). Since the disease is typically unilateral or confined to local areas, it seems that the developmental difficulty is a local disease or dysfunction rather than a hormonal one, as in osteitis fibrosa cystica (von Recklinghausen's disease). Therefore, from a theoretical view, there seems little to recommend the use of either cortisone or pituitary adrenocorticotropic hormone in the treatment of this condition. As in this case, when fractures occur, the lesion usually heals. In regions where a large amount of bone has been replaced by fibrous tissue, the fibrous tissue may need to be curretted out and chips of cancellous bone used to produce strong bone. At present, other treatment has little to offer.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

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ACNE PRODUCED BY IODIDES

TO THE EDITOR:—*A man suffering from bronchial asthma for five years has evening and night attacks every day. The only medicine which helps is saturated solution of potassium iodide. However, after three days of this treatment, acne with boils develops on the face. The use of hydriodic acid has the same complication. Can anything be done to prevent acne? Would it be worth while to try thyroid extract or a drug to suppress thyroid, like thiouracil? Is banthine® helpful in asthma? Is there any relation between serum cholinesterase and asthma?*

E. E. Sheldon, M.D., New York.

ANSWER.—There is no certain method of preventing the acne produced by iodides. The eruption will not be prevented by the use of enteric coating, organic iodine or any other method that will affect the absorption of the iodine radical. In many cases, if the iodides are continued, the eruption ultimately disappears. The addition of potassium arsenite (Fowler's) solution has been thought to modify this tendency. The beneficial effect of iodine is due to its direct effect on the mucous glands of the bronchi. It is obvious, therefore, that neither thyroid extract nor thiouracil would act in a similar manner. Asthmatic patients who cannot tolerate iodides will frequently obtain benefit from expectorant doses of ipecac or ammonium chloride.

Banthine® (beta-diethylaminoethyl xanthene-9-carboxylate-methabromide) has an action very much like atropine and is not likely to produce much benefit in asthma. Cholinesterase serum levels have not been shown to be affected in asthma. There is no certain method of increasing the cholinesterase blood level. Epinephrine is, of course, the most reliable sympathomimetic in asthma. Methoxyphenamine (orthoxine®) hydrochloride is another drug that has been recently demonstrated to be useful in asthma.

ASTHMA, THE SALIVARY GLANDS AND POTASSIUM IODIDE

TO THE EDITOR:—*A patient with asthma has been getting fairly good relief with ephedrine. On several occasions I have prescribed potassium iodide. Each time, after about 36 hours and only after a dosage of 0.3 cc. three times a day had been reached, his parotid and submaxillary glands would swell and become tender. His appearance would be that of a person with mumps. On withdrawal of the medication, this swelling would recede. Also, on each occasion, his asthma, which is of the chronic type, would be benefited. Could you enlighten me as to the reason for this peculiar reaction?* *M.D., Pennsylvania.*

ANSWER.—One of the normal actions of iodide is to stimulate mucus and serous glands. It is due to this hypersecretion of a thin fluid by the mucus glands of the bronchi that benefit in asthma is obtained. This same action results in overactivity of the salivary glands. With excessive doses of iodides, a large percentage of persons will experience many undesirable symptoms, including swelling of the salivary glands. With the usual therapeutic doses employed in asthma, about 2 gm. a day, about one in 50 will react with salivary gland swelling. This is not in the nature of an allergic phenomenon but rather an exaggerated response of the normal physiological effect of the drug.

THE WHIPPLE PRINCIPLE

TO THE EDITOR:—*It is my understanding that the "Whipple principle" is valuable in the treatment of secondary anemia. Has it ever been utilized?*

Frank C. Beall, M.D., Fort Worth, Texas.

ANSWER.—Whipple and Walden (*Am. J. M. Sc.* **179**:628 [May] 1930) described a liver fraction potent in anemia due to hemorrhage in dogs. This extract, sometimes referred to as the "Whipple principle," is "the portion insoluble in 70% alcohol dried and designated the secondary anemia fraction." Although the value of this fraction in "secondary" anemia of man has not been adequately demonstrated, it has been available commercially through Eli Lilly & Company and is probably the liver component of at least some of the liver and iron products now available.

TOXIC GASES FROM GLASS MELTING

TO THE EDITOR:—*In the process of glass melting one "charge" consists of cullet (broken glass), sodium carbonate, sodium sulfate, manganese and calcium fluoride—this entire mixture coming in contact with the side wall material of silica. Despite the ventilation system, gases are present in the surrounding area. The men working near the glass melting process are, of late, complaining of mild conjunctivitis, lacrimation, burning sensation of nasal mucous membrane, cough, dermatitis and nausea. It is thought that the combustion product silicon fluoride is the causative agent. Is silicon fluoride the sole irritant? What concentration of silicon fluoride in the air would be needed to cause irritation? What other combustion products would be irritating? How serious or dangerous is silicon fluoride?* *Clarence T. Risley, M.D., Conneaut, O.*

ANSWER.—This query implies but does not state that only one of several possible "charges" is associated with the disturbances described. On that assumption the two likely variables are the manganese and the calcium fluoride. However, the manipulation of any and all batches could be associated with irritants. The gas fuel could lead to irritant sulfur compounds, aldehydes and acrolein. Both infrared and ultraviolet rays are emitted by the molten metal (glass). Prior to the molten state, dusts from the fines of the charge arising in the process of introduction into the pots provide irritants. Sodium carbonate dust is a prospective offender. The manganese dioxide will not produce the manifestations described but is occasionally the source of a severe central nervous system disease. This is more likely to arise in the batch or mix house. If the difficulty truly springs from the molten metal, the cause probably is sodium fluoride. The calcium fluoride may be altered to the sodium salt, the sodium being furnished by the sodium carbonate. This fluoride is more volatile than other common ones. The action of this fluoride is likely to be limited to just the abnormalities mentioned. In industry neither acute nor chronic systemic fluoride poisoning is frequent. Surface irritation is frequent. The maximum allowable concentration is 2.5 mg. per cubic meter of air. Obviously this is not a stringent standard allowance. On an over-all appraisal it may be stated that no single precise substance is responsible and instead that multiple influences contribute, including rays, gas combustion products, heat, and dust.

CASTS ON A LIMB

TO THE EDITOR:—*What are the indications for the use of the Wilkie boot? Are casts ever kept on a limb too long? What are the indications for taking them off?*

M.D., New York.

ANSWER.—The Wilkie boot has been largely given up in this country but is still useful in patients who are poor operative risks, especially with serious heart lesions.

Absorption varies with the type of fracture or infection and whether an accurate apposition of the hip has been made.

A cast can be kept on a limb too long, but indications for taking off a cast depend on the condition for which it is applied. In rheumatoid arthritis, the cast must be removed every day for a period of time. In fractures, it should be left on until the fracture is firm.

YAWNING DURING SLEEP

TO THE EDITOR:—*What is the significance of frequent yawning during deep sleep in a child of 7 who is normal in every way?*

R. R. Snook, M.D., McLouth, Kan.

ANSWER.—Frequent yawning during sleep probably has no great significance. It may indicate a mild sleep disturbance, causing lighter sleep than normal, which may be the result of too much excitement just before bedtime (as from watching television), an evening meal that was too heavy or some daytime behavior difficulties carried over into sleep. In the absence of any other symptom or physical or emotion observations, it is impossible to know the cause. It might be called a sleep tic, various ones of which have been described.

SERUM SICKNESS

To the Editor:—*A man injured his finger and, after a test for serum sensitivity, received a prophylactic injection of tetanus antitoxin. He had received an injection of tetanus antitoxin five years previously. Two weeks after the injection, generalized muscular and joint pain developed. Two weeks later, he was found to have acute nephritis. He had 5% eosinophils, but no local or general skin manifestation. His blood pressure was normal at that time. The result of the heterophil antibody test was positive. Five months later, his blood pressure was 190/105, his heart was enlarged to the anterior axillary line, and he had pitting edema of the ankles. Urinalysis revealed a specific gravity of 1.010, 2 + albumin, 4 to 6 white cells, innumerable red blood cells, and granular casts. He had retinal hemorrhages. Blood urea on two occasions was recorded as 46 and 32 mg. per 100 cc. Serum chlorides were 106, serum calcium was 4.8, and serum phosphorus 2.1 mg. The serum albumin-globulin ratio was 3.1 to 2.3 gm. Phenolsulfonphthalein excretion was 27% in two hours. A muscle biopsy was negative for changes indicative of periarteritis nodosa. Are the above findings compatible with a diagnosis of (1) serum sickness with resulting periarteritis nodosa and nephritis or (2) acute inflammatory rheumatism with cardiovascular renal disease caused by antitoxin?* *M.D., Virginia.*

Answer.—The history of previous administration of tetanus antitoxin and the description of symptoms which followed by two weeks the injection of tetanus antitoxin after the finger injury strongly suggest serum sickness. The fact that a muscle biopsy was negative does not exclude periarteritis nodosa. The first diagnosis proposed seems to be the correct one.

EFFECTS OF SMOKING

To the Editor:—*Please tell me if any work has been done on the effect of smoking on (1) acidity of the stomach, (2) basal metabolic rate, and (3) sugar content of the blood.*

H. W. Nottley, M.D., White Plains, N. Y.

Answer.—Gastric hyperacidity has been reported following smoking, both as an effect of the nicotine on the nerve centers and as a local reaction to the irritating swallowed constituents of the smoke. Basal metabolic rate changes resulting from smoking have not been described. A rise in the blood sugar content of the blood following smoking has been repeatedly observed and has been ascribed to stimulation of epinephrine secretion by nicotine. Conflicting results have been reported as a result of the use of insufficient dosage or controls. Further information may be obtained in Schrumpf-Pierron (Tobacco and Physical Efficiency: Digest of Clinical Data, New York, Paul B. Hoeber, 1927), Gray (Tobacco Smoking and Gastric Symptoms, *Ann. Int. Med.* **3**:267 [Sept.] 1929), and Haggard and Greenberg (Effects of Cigaret Smoking upon Blood Sugar, *Science* **79**:165 [Feb. 16] 1934).

MENSTRUATION AT THE MENOPAUSAL AGE

To the Editor:—*What is the proper management of a woman in the menopausal age who is essentially normal on physical examination but who complains of frequent or heavy menstrual periods?*

M.D., California.

Answer.—Generally, surgical treatment is neither required nor satisfactory for frequent or heavy menstrual periods near the menopause. In most women the bleeding ceases completely without the necessity for surgical therapy. Of course, if there is any bleeding between the periods, cancer must be ruled out by curettage and cervical biopsy.

If the menstrual periods are so profuse that the patient must go to bed, curettage should be performed in the hope that it will stop the profuse bleeding until the menopause occurs. If curettage is unsuccessful, one has a choice of irradiation or hysterectomy, preferably through the vagina. Opinion is divided on this subject. Several gynecologists have abandoned irradiation for benign uterine bleeding at the menopause, because in some cases cancer of the endometrium appears several years later.

SLEEPING PILLS

To the Editor:—*I see an increasing number of patients who tell me that they have been taking sedatives at bedtime for years, some as long as 15 years; the usual sedative is pentobarbital (nembutal®) sodium. What harm could come from such long usage? What is your opinion of the use of sedatives in the coronary patient? None of these persons seems to be a true addict, but they feel that the use of a "sleeping pill" is better than fighting sleep.* *M.D., Illinois.*

This inquiry was referred to two authorities, whose respective replies follow.—Ed.

Answer.—It is only occasionally that the use at bedtime of a sedative such as pentobarbital (nembutal®) sodium leads to an untoward result. Long use of a small dose is not harmful. For pathological changes to be produced in the central nervous system, it is necessary to give very large doses of a barbiturate over a period as long as a week. Occasionally a patient who is not stable emotionally will take an overdose of a barbiturate with suicidal intent, but it is unlikely that a physician would prescribe barbiturates for such a person for very long. Small doses of barbiturate for persons who have coronary disease are justified by the rest that the patient obtains thereby. A few persons have an idiosyncrasy to barbiturates that prevents them from obtaining any real benefit from them; that is, such persons may become excited rather than quieted by the drug.

Answer.—As long as modern civilization makes life strenuous, many persons will need help in getting sleep. Some experts say they have seen patients who appeared to be typically habituated to sleeping pills; however, according to one observer, in 45 years of busy practice, he has seen no harm from the long-continued use of sleep-makers. During these years he has seen only a few persons who were taking excessive amounts of these drugs, and they were all psychopaths when they began taking the drugs. They were able to stop the use of the drugs without difficulty. Nervous persons should take sleeping pills only at night when they need them.

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MULTIPLE MOLES

To the Editor:—*A white woman, married, 25, has small pigmented moles scattered on her body. In the past two years, two small nevi have been removed because of recent appearance and increase in size—one from the palm of the hand, 1 mm. in diameter, and one from the shoulder, 3 mm. in diameter. She now has a pigmented mole, about 3 mm. in diameter, on the skin of the antecubital fossa; this has doubled in size in about one month. The pathological report on two excised lesions was "junction nevus, no malignant change." 1. Should each pigmented mole that increases in size be removed? 2. What is the prognosis? 3. Will pregnancy have an unfavorable effect?* *M.D., Virginia.*

Answer.—The junction-type nevus is one that is prone to become malignant. Not all such nevi do become malignant, so that opinion is divided as to whether they should be excised routinely. When they show signs of activity, however, such as change in size, shape, or color, or if they are situated in areas that are subjected to repeated irritation, the better course is to excise them. It is impossible to predict whether pregnancy will have an unfavorable effect on the lesions. It should be remembered that nearly all persons have at least one mole somewhere on the body, so that the incidence of malignant change in them must be very low.

TERRAMYCIN

To the Editor:—*Are there any contraindications for the intraperitoneal administration of terramycin solutions?*

H. J. Denman, M.D., Warm Springs, Ore.

Answer.—A search of current literature does not reveal the indications or the contraindications for the administration of terramycin solutions by the intraperitoneal route.